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TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

THIRTY-SECOND SESSION

HELD AT THE MORAINE HOTEL, HIGHLAND PARK, ILL.
MAY 31, JUNE 1 AND 2, 1920

EDITED BY

OSCAR M. SCHLOSS, M.D.

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VOLUME XXXII

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PRESIDENTS

1889. A. Jacobi, M.D.
1890. J. Lewis Smith, M.D.
1891. T. M. Rotch, M.D.
1892. William Osler, M.D.
1893. A. D. Blackader, M.D.
1894. John M. Keating, M.D.
1895. F. Forchheimer, M.D.
1896. Joseph O'Dwyer, M.D.
1897. Samuel S. Adams, M.D.
1898. L. Emmett Holt, M.D.
1899. William P. Northrup, M.D.
1900. Henry Koplik, M.D.
1901. William D. Booker, M.D.
1902. W. S. Christopher, M.D.
1903. J. P. Crozer Griffith, M.D.
1904. Augustus Caillé, M.D.
1905. C. G. Jennings, M.D.
1906. A. Jacobi, M.D.
1907. B. K. Rachford, M.D.
1908. C. G. Kerley, M.D.
1909. Charles P. Putnam, M.D.
1910. David L. Edsall, M.D.
1911. Henry Dwight Chapin, M.D.
1912. Walter Lester Carr, M.D.
1913. John Lovett Morse, M.D.
1914. Samuel McC. Hamill, M.D.
1915. George N. Acker, M.D.
1916. Rowland G. Freeman, M.D.
1917. Frank Spooner Churchill, M.D.
1918. Linnaeus E. La Fétra. M.D.
1919. Edwin E. Graham, M.D.
1920. Thomas S. Southworth, M.D.

OFFICERS, 1920

President.....Thomas S. Southworth, M.D.
Vice-President.....Alfred Hand, Jr., M.D.
Secretary.....Howard Childs Carpenter, M.D
Treasurer.....Charles Hunter Dunn, M.D.
Recorder and Editor.....Oscar M. Schloss, M.D.

COUNCIL

D. Murray Cowie, M.D., *Chairman*

L. Emmett Holt, M.D.
Charles A. Fife, M.D.
Royal S. Haynes, M.D.
Julius P. Sedgwick, M.D.
Isaac A. Abt, M.D.
Richard M. Smith, M.D.

MEETING PLACES

1888. Washington, D. C. (Organization), September 18.
1889. Washington and Baltimore, September 20 and 21.
1890. New York, June 3 and 4.
1891. Washington, September 22 and 25.
1892. Boston, May 2, 3 and 4.
1893. West Point, N. Y., May 24, 25 and 26.
1894. Washington, May 29 and June 1.
1895. Virginia Hot Springs, May 27, 28 and 29.
1896. Montreal, May 25, 26 and 27.
1897. Washington, May 4, 5 and 6.
1898. Cincinnati, June 1, 2 and 3.
1899. Deer Park, June 27, 28 and 29.
1900. Washington, May 1, 2 and 3.
1901. Niagara Falls, May 27, 28 and 29.
1902. Boston, May 26, 27 and 28.
1903. Washington, May 12, 13 and 14.

1904. Detroit, May 30, 31 and June 1.
1905. Lake George, N. Y., June 19, 20 and 21.
1906. Atlantic City, N. J., May 30, 31 and June 1.
1907. Washington, May 7, 8 and 9.
1908. Delaware Water Gap, May 25, 26 and 27.
1909. Lenox, Mass., May 27 and 28.
1910. Washington, May 3, 4 and 5.
1911. Lake Mohonk, N. Y., May 31 and June 1 and 2.
1912. Hot Springs, Va., May 29, 30 and 31.
1913. Washington, May 5, 6 and 7.
1914. Stockbridge, Mass., May 26, 27 and 28.
1915. Lakewood, N. J., May 24, 25 and 26.
1916. Washington, May 8, 9 and 10.
1917. White Sulphur Springs, W. Va., May 28, 29 and 30.
1918. Lenox, Mass., May 27, 28 and 29.
1919. Atlantic City, N. J., June 16, 17 and 18.
1920. Highland Park, Ill., May 31, June 1 and 2.

OFFICERS, 1921

President.....John Howland, M.D.
Vice-President.....R. Langley Porter, M.D.
Secretary.....Howard Childs Carpenter, M.D.
Treasurer.....Charles Hunter Dunn, M.D.
Recorder and Editor.....Oscar M. Schloss, M.D.
Member of Executive Committee on Arrangements of the Congress of American Physicians and Surgeons.....J. P. Crozer Griffith, M.D.
Alternate.....Samuel S. Adams, M.D.

COUNCIL

L. Emmett Holt, M.D., *Chairman*

Charles A. Fife, M.D.
Royal S. Haynes, M.D.
Julius P. Sedgwick, M.D.
Isaac A. Abt, M.D.
Richard M. Smith, M.D.
Henry L. K. Shaw, M.D.

ACTIVE MEMBERS

1903. Abt, Isaac A., M.D.....815 Monroe Bldg., Chicago
1893. Acker, George N., M.D.....913 Sixteenth Street, Washington
O Adams, Samuel S., M.D.....1801 Connecticut Avenue., N.W., Washington
1916. Bartlett, Frederic H., M.D.....44 East Sixty-Third Street, New York
O Blackader, A. D., M.D.....236 Mountain Street, Montreal
1916. Blackfan, Kenneth D., M.D.....Johns Hopkins Hospital, Baltimore
1911. Bowditch, Henry I., M.D.....86 Bay State Road, Boston
1918. Brennemann, Joseph, M.D.....5626 Dorchester Avenue, Chicago
1911. Butterworth, Wm. W., M.D..1222 Maison Blanche Bldg., New Orleans
O Caillé, Augustus, M.D.....753 Madison Avenue, New York
1911. Carpenter, Howard C., M.D.....1805 Spruce Street, Philadelphia
O Carr, Walter Lester, M.D.....68 West Fifty-First Street, New York
O Chapin, Henry Dwight, M.D...51 West Fifty-First Street, New York
1897. Churchill, F. S., M.D.....106 Marlborough Street, Boston
1920. Cooley, Thomas, M.D.....90 Forest Ave., Detroit
1909. Cowie, D. M., M.D.....Lawrence Building, Ann Arbor, Mich.
1917. De Buys, L. R., M.D.....Maison Blanche Bldg., New Orleans

1906. Dunn, Charles Hunter, M.D.....178 Marlborough Street, Boston
1904. Eaton, Percival J., M.D....715 N. Highland Avenue, E.E., Pittsburgh
1907. Fife, Charles A., M.D.....2033 Chestnut Street, Philadelphia
1918. Fleischner, E. C., M.D.....350 Post Street, San Francisco
1895. Freeman, Rowland G., M.D..211 West Fifty-Seventh Street, New York
1913. Friedlander, Alfred, M.D.....4 West Seventh Street, Cincinnati
1913. Gerstenberger, Henry, J., M.D.....1940 Noble Road, Cleveland
1910. Gittings, J. C., M.D.....1805 Pine Street, Philadelphia
1897. Graham, E. E., M.D.....1713 Spruce Street, Philadelphia
1892. Griffith, J. P. Crozer, M.D.....1810 Spruce Street, Philadelphia
1917. Grulee, Clifford, M.D.....104 South Michigan Avenue, Chicago
1898. Hamill, S. McC., M.D.....1822 Spruce Street, Philadelphia
1902. Hand, Alfred, Jr., M.D.....1724 Pine Street, Philadelphia
1910. Haynes, Royal S., M.D.....140 West Fifty-Eighth Street, New York
1909. Heiman, Henry, M.D.....64 West Eighty-Fifth Street, New York
1914. Helmholz, Henry F., M.D.....800 Davis Street, Evanston, Ill.
1910. Herrman, Charles, M.D...250 West Eighty-Eighth Street, New York
1915. Hess, Alfred F., M.D.....16 West Eighty-Sixth Street, New York
O Holt, L. Emmett, M.D.....14 West Fifty-Fifth Street, New York
1913. Hoobler, B. Raymond, M.D.....1563 David Whitney Building, Detroit
1905. Howland, John, M.D.....20 East Eager Street, Baltimore
1918. Jeans, Philip C., M.D.....500 South Kingshighway, St. Louis
1896. Kerley, Charles G., M.D....132 West Eighty-First Street, New York
1905. Knox, J. H. Mason, Jr., M.D.....“The Severn,” Baltimore
O Koplik, Henry, M.D.....30 East Sixty-Second Street, New York
1903. Ladd, Maynard, M.D.....535 Beacon Street, Boston
1903. La Fétra, Linnaeus E., M.D....113 East Sixty-First Street, New York
1911. Lucas, William Palmer, M.D..University of California, San Francisco
1912. McClanahan, H. M., M.D.....507 McCague Bldg., Omaha
1909. Machell, H. T., M.D.....459 Avenue Road, Toronto
1917. Marriott, W. McKim, M.D.....Washington University, St. Louis
1898. Miller, D. J. Milton, M.D...Pacific and California Aves., Atlantic City
1918. Mitchell, A. Graeme, M.D.....1717 Pine Street, Philadelphia
1896. Morse, J. Lovett, M.D.....70 Bay State Road, Boston
O Northrup, William P., M.D..61 East Seventy-Third Street, New York
1915. Park, Edwards A., M.D.....Johns Hopkins Hospital, Baltimore
1910. Pisek, Godfrey R., M.D.....26 East Sixty-Fourth Street, New York
1912. Porter, R. Langley, M.D.....240 Stockton Street, San Francisco
1891. Rachford, B. K., M.D.....1961 Madison Road, Cincinnati
1917. Ramsey, Walter R., M.D.....942 Lowry Building, St. Paul, Minn.
1905. Ruhräh, John, M.D.....11 East Chase Street, Baltimore
1900. Saunders, E. W., M.D.....1541 South Grand Avenue, St. Louis
1912. Schloss, Oscar M., M.D.....39 East Sixty-First Street, New York
1917. Schlutz, F. W., M.D.....16 LaSalle Bldg., Minneapolis
1913. Sedgwick, Julius P., M.D.....2015 Kenwood Parkway, Minneapolis
1902. Shaw, Henry L. K., M.D.....361 State Street, Albany
1914. Sherman, DeWitt H., M.D.....680 West Ferry Street, Buffalo
1920. Smith, Charles Hendee, M.D...66 West Fifty-Fifth Street, New York
1915. Smith, Richard M., M.D.....355 Marlborough Street, Boston
1891. Snow, Irving M., M.D.....737 Delaware Avenue, Buffalo
1905. Southworth, Thomas S., M.D.....807 Madison Avenue, New York
1911. Talbot, Fritz B., M.D.....311 Beacon Street, Boston
1919. Taylor, Rood, M.D.....614 Syndicate Building, Minneapolis
1914. Van Ingen, Philip, M.D....125 East Seventy-First Street, New York
1912. Veeder, Borden S., M.D.....608 Humboldt Building, St. Louis
1914. Walls, Frank X., M.D.....1208, 30 North Michigan Ave., Chicago
1896. Westcott, Thompson S., M.D.....1720 Pine Street, Philadelphia
1913. Wilcox, Herbert B., M.D.....39 East Seventy-Fifth Street, New York
O Winters, J. E., M.D.....25 West Thirty-Seventh Street, New York

Note.—The first column gives the date of election to the Society. The organizers of the Society are designated by “O,” the date being 1888.

HONORARY MEMBERS

Dr. John Thompson.....Edinburgh, Scotland
Dr. George F. Still.....London, England
Dr. V. Hutinel.....Paris, France
Dr. Charles Rauchfuss..... Petrograd, Russia
Dr. P. F. Armand-Delille.....Paris, France
Dr. A. Marfan.....Paris, France
Dr. Leonard Findlay.....Glasgow, Scotland
Dr. Truly King.....New Zealand
Dr. E. Weill.....Lyons, France
Sir Arthur Newsholme.....London, England

EMERITUS MEMBERS

Dr. Allen Baines .....Toronto
Dr. John Dorning .....New York
Dr. Francis Huber .....New York

Deceased

JOHN A. JEFFRIES, M.D.
Born, September 2, 1859,
Died, March 26, 1892.

THOMAS F. SHERMAN, M.D.
Born, March 17, 1856,
Died, September 26, 1893.

JOHN M. KEATING, M. D.
Born, April 20, 1852,
Died, November 17, 1893.

CHARLES WARRINGTON EARLE, M.D.
Born, 1845,
Died, November 19, 1893.

J. LEWIS SMITH, M.D.
Born, October 15, 1827,
Died, June 9, 1897.

JOSEPH O'DWYER, M.D.
Born, October 12, 1841,
Died, January 7, 1898.

JOHN HENRY FRUITNIGHT, M.D.
Born, November 9, 1851,
Died, December 18, 1900.

FREDERICK A. PACKARD, M.D.
Born, November 17, 1862,
Died, November 1, 1902.

WALTER S. CHRISTOPHER, M.D.
Born, 1859,
Died, March 2, 1905.

LEROY MILTON YALE, M.D.
Born, February 12, 1841,
Died, September 12, 1906.

JAMES PARK WEST, M.D.
Born, June 27, 1858,
Died, June 25, 1908.

FREDERICK FORCHHEIMER, M.D.
Born, 1853,
Died, June 1, 1913.

THOMAS MORGAN ROTCH, M.D.
Born, 1850,
Died, March 9, 1914.

CHARLES P. PUTNAM, M. D.
Born, 1845,
Died, April 22, 1914.

HENRY LEBER COIT, M.D.
Born, 1854,
Died, March 13, 1917.

ABRAHAM JACOBI
Born, May 6, 1830,
Died, July 10, 1919.

FLOYD CRANDALL
Born, May 2, 1858
Died, Nov. 19, 1919

ABRAHAM JACOBI

One of the remarkable men of medicine, a charter member of this Society, its first president, and the only member who has ever been honored by having been twice chosen as its president — Dr. Abraham Jacobi, has finished his inspiring work.

Dr. Jacobi had certain rare and striking characteristics. His personality was distinguished. His gentleness was almost feminine yet with it he had a forcefulness that was impelling. His broad human interest, his love of men, his interest in their welfare and his eagerness to help those who needed help, were known to all of us. With his profound learning, his great wisdom, his broad experience, his knowledge of the world and his gentle tact, he was a rarely qualified advisor.

Perhaps one of the most beautiful things in Dr. Jacobi's beautiful life was his perennial youth. This youthful spirit was born of contact with youth. Dr. Jacobi lived where he could serve most, and he knew that the receptive field for the ideas and ideals he wished to implant was in the mind of youth. Therefore, he made young men his companions that he might the more easily guide them toward the higher and better things.

He who serves much is loved much. The multitudes that Dr. Jacobi served, loved him.

Whilst we, the members of the American Pediatric Society, mourn his death and deeply regret his going, we are profoundly grateful to Almighty God that He gave such a man to the world, and that we were privileged to sit at his feet, learn of his wisdom, and be numbered among his friends.

S. McC. Hamill,
(Signed) S. S. Adams,
R. S. Haynes.

FLOYD M. CRANDALL

In the death of Dr. Floyd M. Crandall the American Pediatric Society has suffered the loss of a member whose interest and whose faithful services will long be remembered.

One of the oldest members of the Society, for many years most assiduous in the fulfilment of the duties of recorder-editor, member of the Council and vice president, he brought to the meetings of the Society and the conduct of its affairs a ripe judgment, a broad experience, a moderation and a devotion which will not soon be forgotten. Of late, as emeritus member, though less closely in contact with the affairs of the Society, the influence of his benign personality yet has been constantly felt by his successors as the memory of his character and achievements will be gratefully cherished in the hearts of all.

It is with an acute sense of its own loss that the Society turns to Dr. Crandall's family to assure them and the community of our sorrow and our appreciation of the privilege long enjoyed and regretfully relinquished of having in our midst one of so accomplished a mind, so ardent a spirit, so whole a character.

Therefore, it is resolved that this Resolution be spread on the Minutes of the Thirty-Second Annual Meeting of the American Pediatric Society and a copy be transmitted to Dr. Crandall's family with the assurance of our truest sympathy.

S. McC. Hamill,
(Signed) S. S. Adams,
R. S. Haynes.

CONSTITUTION AND BY-LAWS OF THE AMERICAN PEDIATRIC SOCIETY

ARTICLE I

Name and Object of the Society

The Society shall be known as the American Pediatric Society, and shall hold an annual meeting.

It has for its object the advancement of the knowledge of physiology, pathology and therapeutics of infancy and childhood.

ARTICLE II

Proceedings

The proceedings shall consist of:

1. Discussions on subjects previously selected.
2. Original communications.
3. Demonstrations of gross and microscopic preparations, apparatus, and instruments.

ARTICLE III

Members

The Society shall be composed of three classes of members to be designated: (1) active members; (2) emeritus members, and (3) honorary members.

The number of active members shall be limited to eighty-five.

The number of emeritus members shall be unlimited.

The number of honorary members shall be limited to twenty-five.

ARTICLE IV

Election of Active Members

Nominations to membership, signed by two members of the Society, must be made in writing at least one meeting prior to election.

Nomination should be made to the Secretary, whose duty it shall be to require the nominators to write a personal letter endorsing and stating the qualifications of the nominee, and at the same time furnishing a list of the nominee's professional position and publications, with reprints of the latter, when obtainable.

It shall be the duty of the Secretary to transmit to the Chairman of the Council all the above papers pertaining to each nominee, at least three months prior to his possible election.*

The Chairman of the Council shall transmit the above-named papers to the other members of the Council in the order of their seniority as Council members, the junior members of the Council returning them to the Secretary.

It shall also be the duty of the Secretary to furnish a printed list of all nominees at least once a year to every member of the Society, and it shall be the duty of the members of the Society, without solicitation, to furnish the Council with any information that they may possess as to the fitness of the nominees to become members of the Society.

On nomination by the Council, members shall be elected by the Society by ballot. A two-thirds vote of the members present shall be necessary for election.

ARTICLE V

Election of Emeritus and Honorary Members

Active members who have served fifteen years and have paid all their dues, may on their request and on the recommendation of the Council be made emeritus members. They shall be entitled to attend meetings and read papers, when they so desire, but cannot vote.

Physicians of sufficient eminence to merit the distinction may be elected honorary members, to a number not exceeding twenty-five. Such members shall be entitled to attend all meetings and take part in the proceedings, but cannot vote. Honorary members shall be elected in the same way as active members.

ARTICLE VI

Initiation Fee and Annual Dues

Election to membership shall be completed by the payment of an initiation fee of $10.

Each active member shall pay an annual fee, the amount of which shall be decided at each annual meeting.

Emeritus and honorary members shall be exempt from fees.

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* In the event that required information relating to candidates for membership is not furnished to the Secretary by three months before the time of the meeting at which they would be considered, such candidates for election shall be held over for another year. (Resolution adopted 1912.)

ARTICLE VII

Officers

The officers shall consist of a President, Vice-President, Secretary, Recorder [and Editor], Treasurer and a Delegate to the Congress of Physicians and Surgeons.

The officers shall be elected annually on nomination by the Council.

ARTICLE VIII

Duties of Officers

The duties of the President, Vice-President, Secretary and Treasurer shall be those usual to these offices. The Recorder [and Editor] shall secure the papers read and see that proper notes are taken of the discussion thereon for the use of the committee on publication.

ARTICLE IX

The Council

The Council shall consist of seven members, the senior member being Chairman. One member of the Council shall be elected each year. Four members shall constitute a quorum. The senior member shall retire at the end of each year and shall not be immediately eligible to reelection.

ARTICLE X

Duties of Council

The duties of the Council shall be to consider nominations for membership and report them to the Society. The votes of four members of the Council shall be required for nomination. The Council shall also nominate the officers of the Society and shall decide the time and place of meeting.

ARTICLE XI

Committee of Arrangements

The President, Secretary and the Chairman of the Council shall constitute a committee of arrangements, the President being chairman of this committee. They shall arrange the details of the meeting and the preparation of the program, and they shall have the authority to invite guests to attend the meeting and to participate in the discussion.

ARTICLE XII

Publication Committee

The Secretary, Treasurer and Recorder shall constitute a committee on publication, to which shall be referred all papers, reports and other matters intended for publication.

All papers presented shall become the property of the Society

ARTICLE XIII

Amendments of Constitution and By-Laws

Proposals for amendments of the constitution and by-laws must have been made at the meeting previous to that at which they are voted on, the notice for which shall contain an announcement of the proposed changes. Such changes shall require, for their adoption, an affirmative vote of three-fourths of the active members present.

ARTICLE XIV

Termination of Membership

A member may be expelled from the Society for conduct unbecoming a physician and a gentleman. In such cases, formal charges must be made in writing by two members, which shall be referred to the Council.

Active membership shall lapse for any one of the following reasons:

(1) Absence from two consecutive meetings without excuse acceptable to the Council. The Secretary shall notify members one year before date of possible lapse; (2) non-payment of dues for two years, two notifications having been sent by the Treasurer.

ARTICLE XV

Quorum

Any number of members present at the appointed time of the annual meeting shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for the expulsion of members, or for altering the constitution and by-laws, twenty-five members shall be necessary.

ARTICLE XVI

Order of Business

1. The President shall call the meeting to order and deliver an annual address. In his absence the Vice-President shall preside, and in the absence of all these officers, the Chairman of the Council.

2. When a general discussion is arranged by the Council, the two members appointed to open the discussion shall not occupy more than twenty minutes each; subsequent speakers shall be restricted to ten minutes each.

3. Papers shall not exceed fifteen minutes in the reading. In the discussion following the reading of such papers, remarks shall be limited to five minutes. Should any paper be too long to read in fifteen minutes, the writer must prepare an abstract which can be read within that time.

4. At the business session the report of the Council as a committee on nominations to office and to membership, shall be made, and ballot shall be held thereon.

Adopted May 28, 1900.

MEMBERS OF THE AMERICAN PEDIATRIC SOCIETY AT HIGHLAND PARK, ILL., 1920

MINUTES OF THE THIRTY-SECOND ANNUAL MEETING OF THE AMERICAN PEDIATRIC SOCIETY

Held at the Moraine Hotel, Highland Park, Ill., May 31, June 1 and 2, 1920.

The meeting was called to order at 9:30 a. m. by the President, Dr. Thomas S. Southworth of New York.

The following members were present during the sessions: Drs. Isaac A. Abt, Chicago; George N. Acker, Washington, D. C.; Samuel S. Adams, Washington, D. C.; Frederic H. Bartlett, New York; A. D. Blackader, Montreal; Henry Ingersol Bowditch, Boston; Joseph Brennemann, Chicago; William W. Butterworth, New Orleans; Howard Childs Carpenter, Philadelphia; David Murray Cowie, Ann Arbor, Mich.; L. R. DeBuys, New Orleans; Percival J. Eaton, Pittsburgh; Charles A. Fife, Philadelphia; E. C. Fleischner, San Francisco; Rowland G. Freeman, New York; Alfred Friedlander, Cincinnati; Henry J. Gerstenberger, Cleveland; J. P. Crozer Griffith, Philadelphia; Clifford G. Grulee, Chicago; S. McC. Hamill, Philadelphia; Alfred Hand, Philadelphia; Royal S. Haynes, New York; Henry Heiman, New York; Henry F. Helmholz, Evanston, Ill.; L. Emmett Holt, New York; B. Raymond Hoobler, Detroit; John Howland, Baltimore; P. C. Jeans, St. Louis; Charles G. Kerley, New York; J. H. Mason Knox, Jr., Baltimore; Maynard Ladd, Boston; L. E. LaFétra, New York; H. M. McClanahan, Omaha; W. McKim Marriott, St. Louis; D. J. Milton Miller, Atlantic City, N. J.; A. Graeme Mitchell, Philadelphia; Godfrey R. Pisek, New York; R. Langley Porter, San Francisco; Walter R. Ramsey, St. Paul; E. W. Saunders, St. Louis; Oscar M. Schloss, New York; Frederic W. Schlutz, Minneapolis; Julius P. Sedgwick, Minneapolis; Henry L. K. Shaw, Albany, N. Y.; DeWitt H. Sherman, Buffalo; Richard M. Smith, Boston; Thomas S. Southworth, New York; Fritz B. Talbot, Boston; Rood Taylor, Minneapolis; Philip Van Ingen, New York, and Frank X. Walls, Chicago.

During the meeting the following guests were introduced: Drs. Edward Anderson, Minneapolis; Richard A. Bolt, Baltimore; A. M. Brandt, Bismarck, N. D.; Alan G. Brown, Toronto; H. H. Byfield, Iowa City; J. C. Cartin, Johnstown; William O. Colburn, Lincoln;

W. C. Cole, Minneapolis; Jean V. Cooke, St. Louis; Thomas B. Cooley, Detroit; Clara Davis, Cleveland; J. A. Gardner, La Grange, Ill.; Jesse Gerstley, Chicago; Stanley D. Giffin, Toledo; Otto L. Goehle, Chicago; E. J. Huenekens, Minneapolis; T. C. Hempelmann, St. Louis; Newell Jones, Omaha; Rockwell M. Kempton, Ann Arbor, Mich.; William B. McClure, Evanston, Ill.; W. F. MacNaughton, Detroit; Fred Moore, Des Moines; E. H. Morgan, Toronto; William A. Mulherin, Augusta, Ga.; Eugene W. Murray, Newark, N. J.; M. W. Ott, Minneapolis; A. H. Parmlee, Oak Park, Ill.; Robert Kendig Rewalt, Williamsport, Pa.; Anna E. Rude, Washington, D. C.; Ada E. Schweitzer, Indianapolis; Max Seham, W. R. Shannon and C. A. Stewart, Minneapolis; C. A. Waterbury, Waterloo, Iowa; Walter F. Winholt, Chicago; Allen G. Miller, South Bend, Ind.; S. Amberg, Chicago; M. L. Turner, Des Moines, Iowa; Julius Hess, Chicago; O. W. Rowe, Duluth, and Robert Alfred Black, Chicago.

The reading of the minutes of the thirty-first annual meeting was dispensed with on motion duly seconded and carried.

The following papers were presented:

1. Dr. Thomas S. Southworth, Presidential Address, "Segregation of Pneumonia."

2. Drs. David Murray Cowie and John Purl Parsons: "The Effect of Blood on Picrate Solutions. A Consideration of the Limitations of the Lewis Benedict Test."

The paper was discussed by Drs. Schloss and Cowie.

3. Dr. Linnaeus E. LaFétra: "Epidemic Encephalitis Lethargica."

The paper was discussed by Drs. Freeman, Heiman, Kerley, Howland, Abt, Cowie, Hand, Schloss and La Fétra.

4. Dr. J. P. Crozer Griffith: "Acute Cerebro-Cerebellar Ataxis: With Reports of Cases."

The paper was discussed by Drs. Howland, Ramsey and Griffith.

5. Dr. Isaac A. Abt: "Xanthochromia of the Cerebrospinal Fluid Observed in a Premature Infant."

The paper was discussed by Drs. Hand, Miller and Abt.

6. Dr. Oscar M. Schloss: "The Nature of Reducing Substance in the Urine of Children Suffering from Nutritional Disorders."

The paper was discussed by Drs. Cowie, Heiman, Talbot and Schloss.

7. Dr. Fritz B. Talbot: "Bodily Mechanics. Its Relation to Cyclic Vomiting and Other Obscure Intestinal Conditions."

The paper was discussed by Drs. Kerley, Pisek, La Fétra, Sherman, Miller, Heiman, Smith, DeBuys and Talbot.

8. Dr. A. D. Blackader: "A Brief Case Report on an Epidemic of Hemorrhagic Diarrhea Due to the Streptococcus Mucosus."

The paper was discussed by Drs. Talbot and Blackader.

9. Drs. Borden S. Veeder and T. C. Hempelmann: "The Relation of Phlyctenular Disease to Tuberculosis in Childhood."

The paper was discussed by Drs. Brennemann, Gerstenberger, Talbot, Hoobler and Hempelmann.

10. Dr. Henry Heiman: "A Study of Pneumonia in Infants and Children During the Recent Epidemics."

The paper was discussed by Drs. Pisek, Griffith, Freeman, Brennemann, Blackader, Hoobler, Smith, Saunders and Heiman.

11. Dr. Walter R. Ramsey: "Further Progress in the Study of the Relative Efficiency of the Different Mercurial Preparations in the Treatment of Congenital Syphilis in Infants and Children as Determined by a Quantitative Analysis of the Mercury Elimination in the Urine."

The paper was discussed by Drs. DeBuys, Blackader, Gerstenberger, Fleischner and Ramsey.

12. Drs. P. C. Jeans and Jean V. Cooke: "A Study of the Incidence of Hereditary Syphilis."

The paper was discussed by Drs. Gerstenberger, Brennemann, Heimann, DeBuys, Porter and Jeans.

13. Dr. E. C. Fleischner and K. F. Meyer: "Preliminary Observations on the Pathogenicity for Monkeys of the Bacillus Abortus Bovinus."

14. Dr. J. H. Mason Knox, Jr.: "Lesions in the Mid-brain, with the Report of a Case."

15. Dr. Joseph Brennemann: "The Irritated Meatus in the Circumcised Child."

The paper was discussed by Drs. Kerley, Heiman, Schloss, Marriott, Griffith and Brennemann.

16. Dr. Alfred Hand: "Dyspituitarism So-Called: Absorption of Membranous Bones, Exophthalmos and Polyuria: With Report of Two Cases."

17. Dr. Rowland Godfrey Freeman: "Fresh Vaccines in Whooping-Cough."

The paper was discussed by Drs. Huenekens (by invitation), Fleischner and Freeman.

18. Dr. John Howland: "Some Observations in Rickets." (Lantern slides.)

The paper was discussed by Drs. Marriott, Gerstenberger, Schlutz, Grulee and Howland.

19. Dr. Royal S. Haynes: "The Argonne Association Idea." (Illustrated with lantern slides.)

20. Dr. Henry J. Gerstenberger: "The Factor of the Position of the Diaphragm in Roentgen-Ray Diagnosis of Enlarged Thymus."

The paper was discussed by Drs. Ladd and Freeman.

21. Dr. Rowland Godfrey Freeman: "A Case of Sarcoma of the Kidney."

22. Dr. Oscar M. Schloss: "Cases of Focal Infection in Children."

23. Dr. H. M. McClanahan: "Hypertrophic Stenosis. Failure of Gruel Feeding. Operation. Slight Improvement. Three Cases Doing Nicely, All on Gruel Feeding."

24. Dr. Richard M. Smith: "A Case of Portal Thrombosis in a Child Five Years of Age."

The paper was discussed by Drs. Blackader, Abt and Smith.

25. Dr. W. McKim Marriott: "A Case of Paralysis of the Respiratory Muscles."

The paper was discussed by Drs. Abt, Heiman, Brennemann and Marriott.

26. Dr. Fritz B. Talbot: "Metabolism of an Infant with Sugar Indigestion."

The paper was discussed by Drs. Schloss, Marriott and Talbot.

27. Dr. Henry L. K. Shaw: "Congenital Atresia of the Esophagus."

The paper was discussed by Drs. Grulee, Ramsey, Hoobler and Shaw.

28. Dr. Godfrey R. Pisek: "A Case of Cardio Spasm."

The paper was discussed by Drs. Griffith and Pisek.

29. Dr. Charles A. Fife: "A Case of Sarcoma of the Mediastinal and Retroperitoneal Glands."

30. Dr. L. Emmett Holt: "Primary Sarcoma of the Thymus."

31. Dr. E. F. Fleischner: "Heart Displacement Apparently Due to Mediastinal Emphysema Following Aspiration Pneumonia."

The paper was discussed by Drs. Smith and Fleischner.

32. Dr. David Murray Cowie: "The Duct Sign in Mumps."

The paper was discussed by Drs. Pisek, Talbot, Heiman, Porter, Schlutz and Cowie.

33. Dr. David Murray Cowie: "A Case of Priapism Resulting from Rapidly Spreading Malignant Myxosarcoma with Generalized Metastasis."

34. Dr. Walter R. Ramsey: "Streptococcus Angina with Purpura Hemorrhagica and Multiple Infarcts of the Skin and Subcutaneous Tissues in a Child Two Years Old, Healing Under Dakin's Solution."

The paper was discussed by Dr. Taylor.

35. Dr. Henry J. Gerstenberger: "Report of a Case of Anaphylaxis Following an Intradermal Protein Sensitization Test."

The paper was discussed by Drs. Talbot, DeBuys, Taylor and Gerstenberger.

36. Dr. Howard Childs Carpenter: "Blood Findings in a Child Five Years After Splenectomy."

The paper was discussed by Dr. J. P. Crozer Griffith.

37. Dr. Henry I. Bowditch: "Further Development of Infants' Hospital."

The paper was discussed by Drs. Gerstenberger, Blackader, De Buys, Eaton, Adams, Butterworth and Bowditch.

38. Dr. Charles Gilmore Kerley: "The Effort Syndrome in Children and Young Adults."

The paper was discussed by Drs. Bowditch, Friedlander, Adams, Eaton, Griffith, Brennemann, Abt, Blackader, Miller and Kerley.

39. Dr. L. Emmett Holt: "The Food Requirements of Children After the First Year."

The paper was discussed by Drs. Pisek, Talbot, Hoobler and Smith.

40. Dr. B. Raymond Hoobler: "The Misuse of Milk in the Diets of Infants and Young Children."

The paper was discussed by Drs. Kerley, Smith, Saunders, Ladd, Holt and Hoobler.

41. Dr. Clifford C. Grulee: "Precipitin Reactions to Egg Albumin in the Stools of Infants."

42. Dr. Langley Porter: "Some Observations on the Rôle of Certain Anerobes in the Intestinal Flora of Infants."

The paper was discussed by Drs. Fleischner, Hoobler and Porter.

43. Dr. A. Graeme Mitchell and Dr. Paul A. Lewis: "Some Experiments on the Persistence of Extraneous Bacteria in the Intestinal Tract as Influenced by Diet."

44. Dr. DeWitt H. Sherman: "A Brief Report on Lactic Acid Milk."

The paper was discussed by Drs. Mitchell, Hoobler and Sherman.

45. Dr. E. W. Saunders: "The Urgent Need of Dietetic Reform and the Duty of the Medical Profession Toward All the Young of the Nation."

The paper was discussed by Drs. Hand, Porter and Saunders.

46. Dr. Henry J. Gerstenberger: "Has Malt Soup Extract an Antiscorbutic Value?"

The paper was discussed by Drs. Brennemann, Griffith, Kerley, Gerstenberger, Miller, Southworth and Gerstenberger.

47. Dean G. S. Ford of the Graduate School of the University of Minnesota: "Graduate Work in Pediatrics."

48. Dr. Maynard Ladd: "Medical Supervision of the Boarded-Out Child."

49. Dr. Richard M. Smith: "A Twenty-Four Hour Schedule for a Boys' School."

The paper was discussed by Drs. Talbot, Fleischner, Blackader, Porter, Heiman, Eaton and Smith.

50. Dr. Julius P. Sedgwick: "A Study of Breast Feeding in the City of Minneapolis."

The paper was discussed by Drs. Hoobler, Porter, McClanahan, Gerstenberger, Taylor, Kerley, Fife, Smith and Sedgwick.

51. Dr. Rood Taylor: "The Fate of Subcutaneously Injected Red Blood Cells."

The paper was discussed by Dr. Bartlett.

52. Dr. W. McKim Marriott: "The Circulatory System in Nutritional Disturbances."

The paper was discussed by Drs. Bowditch, Griffith, Schloss and Marriott.

53. Dr. Frederic W. Schlutz: "Recent Studies in Blood Nitrogen of Infants and Children."

54. Dr. Raymond Hoobler: "The Calcium-Magnesium-Phosphorus Balance in Children Subject to Convulsive Disorders."

The paper was discussed by Drs. Bowditch, Griffith, Ladd, Talbot and Hoobler.

55. Drs. Frederick W. Schlutz and Max Scham: "Electrocardiography in Children."

The paper was discussed by Drs. Carpenter and Seham.

The following papers were read by title:

Drs. William Palmer Lucas and J. R. Sharpsteen: "A Comparison of the Theoretical and Actual Energy Needs of New-Born Infants from a Study of 1,000 New-born.

Dr. Charles Hunter Dunn: "The Diagnosis and Prognosis of Tuberculosis in Infancy."

Dr. Charles Herrman: "Heredity as a Factor in the Etiology of the Diseases of Childhood."

Dr. B. K. Rachford: "Congenital Underdevelopment on the Right Side of the Body of an Infant."

Dr. B. K. Rachford: "Malnutrition from Underfeeding in a Two and One-Half Year Old Child."

Drs. William Palmer Lucas and Bradford French Dearing: "Blood Volume in Infants Estimated by the Vital Dye Method."

EXECUTIVE SESSION

June 2, 9 a. m.

The report of the Council was read by the Chairman of the Council, Dr. David Murray Cowie.

The Council recommends the election of Dr. William P. Northrup to Emeritus Membership.

The Council recommends that Dr. Charles Hunter Dunn be excused for absence from this meeting on account of illness.

That all papers presented at this meeting in order to appear in the Transactions must be in the hands of the Recorder by July 1, 1920.

NOMINATION OF OFFICERS

The Council presented the following nominations for officers for the ensuing year:

President: John Howland, Baltimore.

Vice-President: R. Langley Porter, San Francisco.

Secretary: Howard Childs Carpenter, Philadelphia.

Treasurer: Charles Hunter Dunn, Boston.

Recorder and Editor: Oscar M. Schloss, New York.

Member of Council: Henry L. K. Shaw, Albany, N. Y.

Member of Executive Committee, Congress of American Physicians and Surgeons: J. P. Crozer Griffith, Philadelphia.

Alternate: Samuel S. Adams, Washington, D. C.

TIME AND PLACE OF NEXT MEETING

The place of next meeting has been referred to a committee for final action. It will be held a few days before the American Medical Association meeting.

The report of the Treasurer was examined by the Auditing Committee and found correct.

The annual assessment for 1921 will be $15.00.

The transactions are to be published by the American Medical Association.

CHILD HYGIENE

The report of the Committee on Child Hygiene, read by Dr. Richard M. Smith, Boston, was received and recommended for the approval of the Society.

The Council recommended that the retiring Committee on Child Hygiene be reelected for the ensuing year, and that the Committee have advisory rather than executive power.

The Council recommended the reappointment of Richard M. Smith as the Society's representative on the Advisory Committee of the Hygiene Division of the Federal Children's Bureau.

ELECTION OF MEMBERS

The following were recommended for election to membership: Charles Hendee Smith, New York City; Thomas B. Cooley, Detroit.

For honorary membership: Sir Arthur Newsholme, London, England.

The Council recommended that a member be permitted to present not more than one paper at a meeting, and that all papers must be read by members of the Society, except by permission of the Committee of Arrangements.

AMENDMENTS TO BY-LAWS

The Council recommended the adoption of the following amendments to By-Laws:

In Article III: "three classes of members" changed to read "four classes of members." In the second line of this article insert after "2" the words "Associate Members," change "2" and "3" to "3" and "4." At the end of this article add: "The number of Associate Members shall be limited to 15."

A new Article V, to read: The Election of Associate Members. The nomination and election of Associate Members shall be the same as for Active Members. Associate Members to be elected for a period of three years. They may present one paper during the three years.

Old Article V and subsequent articles to be renumbered so as to read "6, 7," etc.

Change Article VI: Insert "active" before the word "membership," and insert "Associate" before the word "Emeritus."

To Article XVI, Section 3, add: All papers must be handed to the Secretary at the time they are presented, and the copy of the discussion by a member must be returned to the Recorder in two weeks from the time it was sent or the discussion will be published as reported.

Article XVI, Section 3, insert: Attendance at the business sessions shall be limited to Active Members.

The report of the Council was accepted by the Society as read.

The amendments to the By-Laws which had been before the Society for one year were read by the Secretary.

It was voted by the Society that these amendments be acted on separately.

The Secretary read the first amendment: "Amend Article III, line, 4, strike out "75" and insert "85"; so that it shall read, "The number of Active Members shall be limited to 85."

It was moved and carried that this amendment be adopted.

The Secretary read the second amendment: "Amend Article XIV, paragraph 2, strike out the word "Three" and insert the word "Two." Strike out the line "(2) failure to present and read a paper for five consecutive years," and the words "in both these cases." The paragraph will then read: "Active Membership shall lapse for any one of the following reasons: (1) Absence from two consecutive meetings without excuse acceptable to the Council. The Secretary shall notify members one year before the date of possible lapse; (2) non-payment of dues for two years, two notifications having been sent by the Treasurer."

It was moved and carried that this amendment be adopted.

The Society voted against the acceptance of the third amendment.

REPORT OF NECROLOGY COMMITTEE

This Committee consisted of Dr. S. McC. Hamill, Dr. S. S. Adams and Dr. R. S. Haynes.

REPORT OF COMMITTEE ON MEMORIAL RESOLUTIONS TO DR. ABRAHAM JACOBI AND DR. FLOYD CRANDALL

It was moved, seconded and carried that the American Pediatric Society express its deep appreciation to the Chicago members and their wives who made the meeting such an enjoyable one. A vote of thanks was extended to Mr. Cushing, the proprietor of the Moraine, to Mr. Larke, the manager of the hotel, and to the managers of the Exmoor Country Club.

It was voted that the American Pediatric Society did not approve of the publication of the Transactions of the Congress of American Physicians and Surgeons as a whole and that the delegate be so instructed.

REPORT OF THE COMMITTEE ON CHILD WELFARE WITH REFERENCE TO THE COURSE FOR MEDICAL STUDENTS

At the meeting of the American Pediatric Society held in Atlantic City, June 16, 17 and 18, 1919, it was voted to create a Committee on Child Welfare. Dr. Richard M. Smith was appointed chairman and was authorized to appoint the other members of the committee. The committee consists of Drs. Samuel McC. Hamill, Henry F. Helmholz, Philip Van Ingen, W. McKim Marriott and Richard M. Smith.

The committee was instructed to prepare a course on child welfare for medical schools and submit the same to the Council for approval. In accordance with this vote the following report is submitted:

The course in Child Welfare or Preventive Pediatrics, as it might be called, should be given in the fourth year of the medical course, and the instruction should be both didactic and practical. The feeding of normal infants and children might be given properly as a part of this course. The time devoted to didactic instruction should be one-sixth of that reserved for instruction in pediatrics and there should be twice as much time given to practical work as to didactic lectures.

The practical work should be given in connection with the infant and child welfare stations and should include the actual care of normal infants and children.

OUTLINE FOR DIDACTIC INSTRUCTION IN PREVENTIVE PEDIATRICS—CHILD WELFARE

I. Definition, scope, etc.

II. Vital statistics:
    1. Importance.
    2. Birth rates.
    3. Infant mortality rates.
    4. Death rates at different ages.

III. Economic background of medicine:
    Influence on health, especially children:
    1. Nationality.
    2. Ignorance.
    3. Climate—season.
    4. Place of residence—city or country.
    5. Financial condition:
        Wages.
        Housing.
    6. Condition of mother:
        Maternal work.
        Age of mother.
    7. Number of children.
    8. Alcohol.
    9. Venereal disease.

IV. Methods of preventive work:
    1. Education:
        Physicians.
        Medical students.
        Trained nurses and nursery maids.
        Public.
    2. Prevention of deaths:
        Important causes.
        Age incidence.
    3. Protection from disease.
    4. Prevention of defects.

5. Provision of means for normal development:
   Food.
   Hygiene—care of body—proper environment.

V. Governmental health agencies:
   Federal:
   The Department of the Treasury—Public Health Service.
   The Department of Labor—Children's Bureau.
   The Department of the Interior—Bureau of Education.
   The Department of Agriculture—Bureau of Chemistry, Bureau of Animal Industry.
   The Department of Commerce—Bureau of Census, Division of Vital Statistics.
   State: Departments of health—child hygiene divisions.
   City and town boards of health.
   Public health nurses.
   Public health laws.
   State hospitals.
   State clinics.
   Rural clinics.
   Traveling exhibits.

VI. Private health organizations:
   American Child Hygiene Association.
   Child Health Organization.
   Other similar organizations.

VII. Details of child hygiene work:
   1. Birth registration.
   2. Prenatal and neonatal care:
      Statistics of stillbirths, fetal deaths, neonatal deaths, deaths from congenital cause and maternal deaths.
      Means of prevention:
      Care of mother during pregnancy—essentials, pregnancy clinics, maternity centers.
      Care of mother at confinement—hospitals.
      Prevention of blindness.
      Maternity insurance.
      Mothers' pensions.
      Midwives.
   3. Infant care:
      Statistics of infant deaths—principal causes, institutional deaths.
      Prevention of deaths and disease:
      Breast feeding.
      Milk and artificial feeding:
      Proprietary foods.
      Hygiene of infancy.
      Baby hygiene stations.
      Prematurity.
      Day nurseries.
      Foundling institutions.
      Boarding-out infants.
      Illegitimacy.

4. Care of child of pre-school age:
   - Statistics of deaths—principal causes.
   - Prevention of deaths and disease:
     - Feeding.:
       - Dietitians.
       - Nutrition classes.
     - Hygiene.
     - Child hygiene stations or welfare centers.
   - Prevention of defects:
     - Teeth.
     - Posture.
     - Adenoids.
     - Tonsils.
     - Rachitis.
5. Care of school child—school hygiene:
   - Statistics of deaths—principal causes.
   - Prevention of deaths and disease:
     - Home—school.
     - Feeding—diets, growth standards, nutrition classes.
     - Care of body.
   - Correction of defects:
     - Teeth—dental clinics.
     - Adenoids.
     - Tonsils.
     - Posture.
     - Hearing.
     - Vision.
   - Special groups:
     - Tuberculosis.
     - Cardiac.
     - Backward.
     - Blind.
     - Deaf and dumb.
     - Crippled.
   - Medical school inspection:
     - School nurses.
     - School clinics.
     - School sanitation—requirements.
   - Open-air schools.
   - Health scouts.
   - Little Mothers' Leagues.
   - Mental hygiene:
     - Normal training—habits.
     - Feebleminded—statistics.
     - Mental examinations.
     - School for feebleminded.
     - State supervision of feebleminded.
   - Recreation:
     - Playgrounds.

4. Adolescence:
   Special problems.

VIII. Child labor:
   Vocational training:
   Health needs of those entering industry.
   Standards of child labor.
   Admissible occupations.
   Present laws.
   Desirable legislation.

RECOMMENDATIONS

It is suggested that the American Pediatric Society send a copy of this report to the professors of pediatrics in all Class A and Class B medical schools and that the following statement accompany the report:

The Committee on Child Welfare of the American Pediatric Society submits the following recommendations for a course in Preventive Pediatrics or Child Welfare:

The last few years have emphasized as never before the necessity for preventive work with children and the recent draft made clear that the practices heretofore in vogue with reference to the care of normal individuals did not produce satisfactory results. If we are to secure a really healthy generation, the work must begin with the children. Physicians must be the ones to give advice. It is extremely desirable for the medical schools to give more definite instruction with reference to the care of normal children and this outline is suggested to this end.

THE SEGREGATION OF PNEUMONIA

THOMAS S. SOUTHWORTH, M.D.
NEW YORK

The study of means for the protection and care of the child has received a tremendous impetus from the world war, and never before has the attention of so many agencies been concentrated upon its problems.

Our country has been peculiarly fortunate in this respect, owing to the foundation which had been laid in former years. Not only had the science and art of pediatrics attained an enviable position of development here; but the purity of our milk supply, the supervision of the child in the school, prenatal care, milk depots, health centers, the prevention of tuberculosis and blindness, the operation of health boards, and all form of social service activity, had advanced to a point where the work exceeded both in amount and excellence that of other countries.

In consequence, we were not only able to spare trained and enthusiastic workers who gave themselves unselfishly to the task of ameliorating the lot of the child on the war torn continent, but were prepared with the insight and trained personnel necessary to embark upon a continent wide crusade on behalf of the child in our own land.

It would be almost impossible to estimate the concrete benefits of the children's year in our national life, and many of the seeds sown will not reach their fullest fruition for years to come. This work will go on, and public conscience once awakened will, with our characteristic national energy, peer into the dark places and demand progress where heretofore there has been little or none.

Already greater attention is being paid to the prevention of infectious diseases, especially of such as bear particularly upon the child. Here, adequate separation of the sick from the well is indispensable, and the principle is capable not only of stricter enforcement, as in rural communities, but of intelligent extension everywhere into new fields. One of these latter I would bring to your attention today.

Pneumonia is admittedly today one of the great endemic plagues of the world, for which less has been accomplished by way of limitation of its ravages than for any other malady of like importance save

pandemic influenza. This has not been due to any lack of interest in the problem, but rather to its complexities, since the processes we call pneumonia are several pathologic entities, of diverse etiology, and with somewhat loosely correlated clinical manifestations. I need enter on no general discussion of the pneumonias of childhood, with which you are all familiar, and of whose direct and indirect mortality you are aware.

Untiring effort has been expended on the pneumonia group in countless laboratories, but while many separate links in the chain of knowledge have been forged, little has been accomplished in welding them together to bind and limit the scourge.

Even in the matter of treatment, if we except the serums developed by Cole, which are as yet little applicable to the young, we are still forced to content ourselves with supporting nature until her time-honored vis medicatrix fails or effects a cure.

Possibly, however, while all energies have been directed to the most serious end of averting catastrophe in the presence of established pneumonic processes, we have not considered so clearly the possibilities of guarding against their inception. We may not have been sufficiently punctilious in taking measures to prevent the individual from becoming infected. Here also the field is a wide one, worthy of further patient study.

But there is one patent avenue which has not been properly guarded. I refer to that of the exposure of susceptible individuals in dangerous propinquity to active cases of the disease. I do not think that this is stating the matter too strongly.

We have in the pneumonias processes caused by the presence of microorganisms of recognized pathogenic virulence. In common with other acute affections of the respiratory tract accompanied by cough, we know that the active micro-organisms of the pneumonias may be distributed within certain limits in the surrounding air by the act of coughing. Yet it has long been our common custom to treat pneumonias in the general wards of our hospitals, and to place about them in the home only the ordinary precautions of the sick room.

It is not only pathetic but humiliating to realize that it required a devastating experience in our military camps with pneumonia in measles and with pneumonia in influenza to force any considerable recognition of the infectiousness of pneumonia. Segregation of such cases may, heretofore, have been practiced by thoughtful physicians,

but the idea had not found its way, and has not yet done so, to the general medical conscience, nor been advocated widely in our literature as a self-evident proposition.

The question may very properly be raised whether, granting the theoretical possibility of such transmission of pneumonia, there is proof that it takes place.

No one questions the contagiousness of smallpox, measles, mumps or whooping cough. The periods of incubation are too definite and the susceptibility too general. This was not so, however, at one time with tuberculosis, in which the period of incubation was long and to which susceptibility was less general.

To demonstrate a new matter convincingly, one must select the most credible instances. Such an one is measles-pneumonia occurring in groups. Years ago, in a children's hospital, I repeatedly had the opportunity, both as physician and pathologist, to observe the incidence of pneumonia in wards quarantined for general outbreaks of measles, and also among groups of children who were segregated as they showed evidence of measles. Whenever pneumonia appeared among such children quarantined for measles, it extended rapidly with an appalling mortality. Such an experience is not readily forgotten.

Similar observations were made in the quarantine pavilion of another institution, and have been confirmed by the reports published by others. I have, therefore, for years insisted, when possible, on the prompt isolation of the first cases of pneumonia among children having measles, with a resulting limitation of the number of cases, and have extended the practice of segregation to all pneumonias.

Others, reviewing their own experience, must have noticed that measles epidemics among grouped children are usually simple, with the exception of the common ear complications, until the appearance of pneumonia changes the picture. They will probably also have observed that during ward epidemics of "colds" or grippe, and even in families, pneumonias occur in groups strongly suggestive of direct infection. There is, however, no reason for believing that susceptibility to infection from pneumonia is limited to those already suffering from measles and other catarrhal processes.

That pneumonia patients should not be allowed to remain in close propinquity to other persons, even those of apparently fairly normal condition, appears scarcely debatable. Yet there is little apparent appreciation of the risk involved in our present lax methods. It has

so long been customary to treat pneumonias in general wards that its propriety seems to be accepted without question. The fresh or open-air treatment of pneumonia has, indeed, happily had the secondary effect of segregating the patients, but I am not aware that it has been advocated for any other reason than the benefit to the patient himself. The employment of the cubical system is a step, though possibly only a step, in the right direction.

During the days of my old hospital internship, scarcely more than three decades ago, patients in advanced stages of pulmonary tuberculosis were treated in the general wards, often occupying beds next to those convalescing from pleurisy and other respiratory affections. Such a disposition would be almost unbelievable today, and shortly afterward, owing to an appreciation of Koch's demonstration of the infectiousness of tuberculosis sputum, such patients were segregated in special wards, and still later in special hospitals. Few infectious disease patients are now allowed to remain in general wards. Typhoid fever and pneumonia constitute the most notable remnant of exceptions.

To allow a patient who has one of the accepted list of quarantinable diseases to remain in contact with a ward or other group of children would be to invoke prompt censure. Not all such cases, however, were formerly considered quarantinable. The matter has been one of slow growth. Naturally those maladies whose infectiousness was most active and most evident were the first to be so treated; then, one after another, but often at considerable intervals, additions have been made to the list. That pneumonia does not as yet appear among them proves little or nothing.

We may grant that comparatively few adults in good health can be shown to have contracted pneumonia while in close attendance on those ill with the disease, but the case is different with infants and young children who are rendered especially susceptible by even slight disturbances of the respiratory tract. Measles, influenza, and the allied grippal affections, as heretofore stated, lead the list, but do not complete it. Young children have little acquired immunity, and the inmates of children's hospitals and institutions are commonly below par. To allow a pneumonia patient to remain in a measles ward is, to my mind, little short of criminal. But if pneumonia is admitted to be transferable in any types of cases, then nothing short of the most complete protective measures for young children, sick or well, is either logical or justifiable.

In attempting to account for a succession of pneumonias in a group, it is not sufficient to say that each case may have been a former passive carrier. This would only be valid in case different types of micro-organisms were proven to be present in each. Here lies an opportunity for important research. But what is the source of the pneumococci found in our respiratory tracts? How do human beings become carriers? Do these organisms come from space, or from other human respiratory tracts, and find a foothold?

If the carrier is a menace both to others and to himself, is it unreasonable to assume that a frank case of pneumonia is an equal or greater menace? Unless we assume the omnipresence of pneumonia organisms in nature, they must be derived from some antecedent contact, direct or indirect. The accepted view appears to be, however, that the active case, the convalescent carrier, and the chronic healthy carrier are most menacing in the order given.

At present we cannot in all probability eliminate the pneumococcus carriers; indeed, no attempts have been made thus far to do so; but it does appear humanly possible to limit the formation of carriers and the direct infection of others by isolating pneumonia patients as soon as they are detected. Until further research establishes more definitely the ways in which pneumonia is spread, and we have not here touched on the possibilities of indirect transference, we cannot be certain of all the etiologic factors; but the less we know of a disease, the greater the obligation to exercise every precaution.

It is probably a safe assumption that there are few present who, two years ago, having in their own person a simple influenza, would have elected to be transferred to a ward containing cases of influenzal pneumonitis; nor who, when their attention had been directed to the possibilities, would put an uncomplicated measles case in the same room with a pneumonia case.

The real question is not whether the case for the infectiousness of the pneumonias is fully proven to the satisfaction of the most skeptical, but whether we are individually to assume the responsibility of permitting exposure to cases of pneumonia which we should not permit to many types of less serious illness, the latter having been declared quarantinable, while pneumonia thus far has not.

The sad experiences of our recent mobilization camps, and the well-known history of primitive or aboriginal communities, serve to remind us that such groups have much of the susceptibility to infec-

tions which are ordinarily more or less limited to childhood. This question of the isolation of pneumonias has, therefore, a wider application than that of our homes and our hospitals.

We are far from possessing valid proofs that cases of pneumonia may be left with impunity among young children or susceptible adults. By doing so, we assume a risk that conditions of which we cannot always be immediately cognizant may at any time greatly augment. Prompt segregation alone eliminates all avenues of danger.

It would, therefore, appear that the obligation is imperative to anticipate the day, to my mind not far distant, when the movement to control pneumonia may make the retention of such cases in a general ward as repugnant to our medical sense of propriety as the retention of an open case of pulmonary tuberculosis.

THE FOOD REQUIREMENTS OF CHILDREN

I. TOTAL CALORIC REQUIREMENTS *

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NEW YORK

In the course of our metabolism observations on young children many interesting facts have been brought out with respect to the general food requirements as to total calories, distribution of the calories as fat, carbohydrate and protein, and other factors in the diet which must be considered. One notes in the literature on the food requirements of growing children a great difference of opinion among the various observers who have studied the subject. Many writers have taken up this problem from only a single point of view, such as the total caloric requirement, or the basal requirement, or the food needs in respect to one or another of the accessory food substances, the so-called "vitamins."

We have, therefore, thought it desirable to consider in its different aspects the whole subject of the food requirements of the child during the entire period of growth.

We shall discuss in this paper the total caloric requirements of children and the different factors which must be reckoned with in estimating the total calories. In succeeding papers we shall take up the proper distribution of the calories of the food as fat, carbohydrate and protein, also other important factors in the diet such as roughage, the difference in growth-promoting properties of the different proteins, the supply of essential inorganic salts and the accessory food substances or vitamins.

At various times and by various authors each of the different factors mentioned has been discussed, but as yet no one has attempted to correlate them all and study the food needs of the child in the entire aspect. The estimates of total caloric requirements of children made by some authors have been purely hypothetical, while others have been based on the requirements of adults.

Observations made during the last few years, especially in this country, have thrown new light on the question of the total calories

* From the laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

needed by the growing child. It is essential to review not only this published work, but also most of the older observations, made chiefly in Germany. From these older observations conclusions have been drawn which do not seem to be warranted either by the number of children studied or the conditions under which they lived. For instance, one author made but a single observation on one child; another's observations were made almost entirely on his own children; those of a third were made on a considerable group of young children who were inmates of an orphan asylum, most of whom were very much under weight; a fourth studied three girls, two of whom were very much over weight.

It is recognized by all who have studied this subject that even in normal healthy children there are very considerable individual variations in food requirements. These variations are certainly much greater in abnormal children or in those studied under unusual conditions. Yet the small number of observations made by some of the German authors referred to are quoted over and over again in textbooks and periodical literature and have been made the basis of very broad and widely accepted deductions. In the light of more recent studies made on a larger scale, some of these deductions seem to be erroneous and misleading.

COMPONENT FACTORS OF CALORIC REQUIREMENTS

In calculating the total caloric requirement of a child there must be taken into account (1) the basal requirement, (2) growth needs, (3) needs for muscular activity, and (4) the food values lost in the excreta. The first of these, the basal requirement, is fairly uniform for children of the same weight. Growth requirements diminish rapidly from birth to the end of the third year and vary but little from this time until the tenth or eleventh year, after which they undergo a marked increase, which is maintained until growth is practically complete. The variation of this growth rate is fairly uniform with all children. Muscular activity, however, varies enormously with different children, but in general tends to increase steadily from birth to puberty. The caloric value of the foodstuff lost in the excreta is subject to very little variation in healthy children of the same age, unless there are marked differences in the diets.

Basal Requirements.—A great deal of accurate information has been accumulated regarding basal requirements, that is, the needs of the body at complete rest. This knowledge has been obtained by calori-

metric observations made by Benedict and Talbot, DuBois, Murlin and others in this country and by Voit and Pettenkoffer, Rubner and Heubner, Schlossman and Murschhauser, and Magnus-Levy and others abroad. Some have based their comparison of individuals on the body surface, but the body weight has been most frequently employed. Many studies have been made of the basal metabolism of adults, both in health and disease, and a large number of observations have been

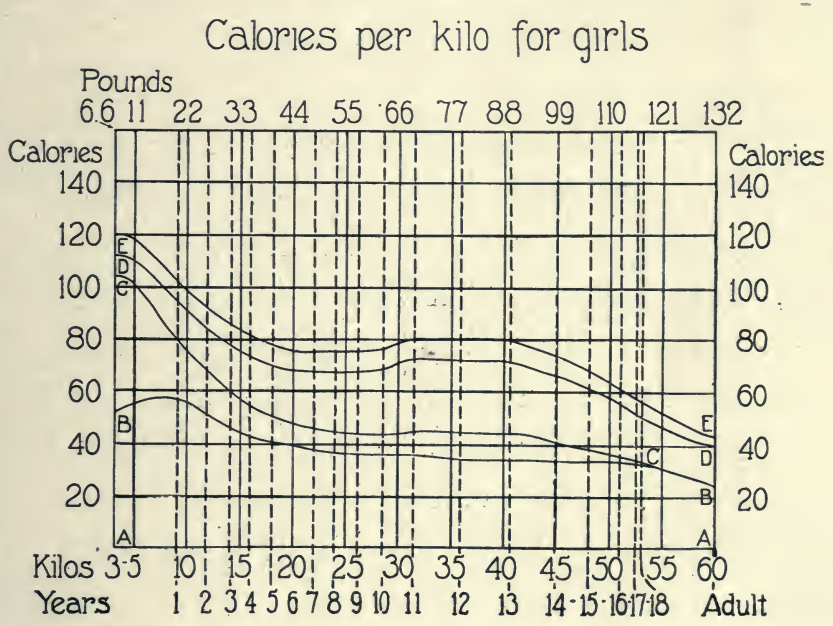

Fig. 1.—The solid vertical lines indicate weights in kilos; the broken lines, approximate weights at each year of age. The space between lines AA and BB shows allowance for basal metabolism; between BB and CC, that for growth; between CC and DD, that for muscular activity; between DD and EE, food values lost in excreta. The space between the lines AA and EE shows the total caloric allowance per kilo.

made on infants, especially the new-born. The intervening period, from the age of one year until the end of puberty, has not been so generally investigated. Talbot and Benedict are the only observers who have studied this entire period systematically.

Benedict [1] has recently presented the results of about 250 observations made by himself and Talbot on children of both sexes, more than

1. Benedict, F. G.: Boston M. & S. J. **181**:107 (July 31) 1919.

half of whom were over one year of age. The range of individual variation in the values obtained was considerable, but the number of observations made is so large that the data seems sufficient to warrant us in accepting their curves as representing the average for the period of growth.[2] They have shown that the basal metabolism per kilo of body weight is at birth "specifically low," that it rises rapidly until the body weight has reached seven to nine kilos and then diminishes slowly to adult life (Charts 1 and 2). There is some difference

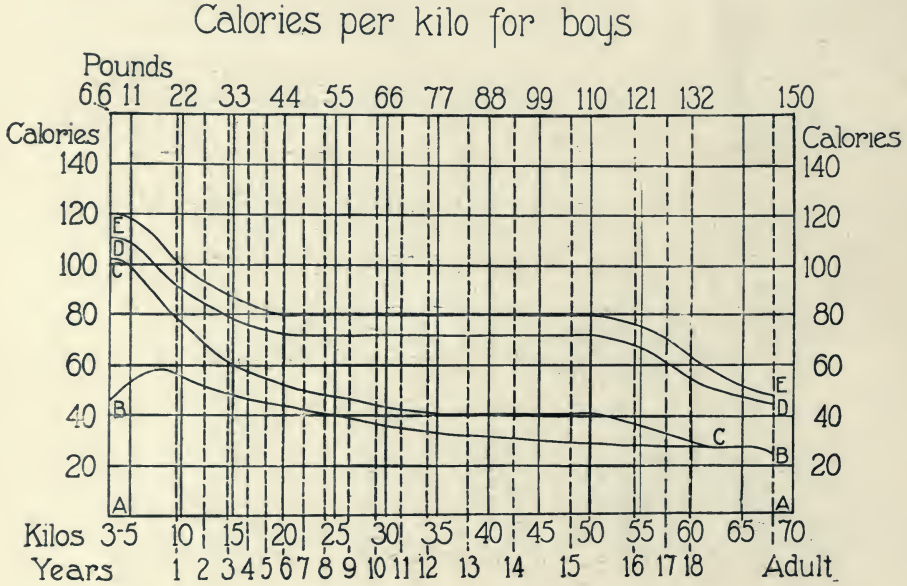

Fig. 2.—The vertical and curved lines have the same significance as in Chart 1.

between the basal needs of boys and girls. After a weight of ten kilos (about one year) is reached the basal requirement of boys exceeds that of girls until a weight of about thirty-five kilos is reached (at about 11 years of age), when the basal needs of girls for a time exceed those of boys. Benedict and Talbot found that the basal caloric requirement increases with age but the relationship is best expressed as calories

2. In a personal communication Talbot stated that the curve for the latter years of childhood may need some revision, since up to the present time the number of observations has not been sufficient to establish definitely this part of the curve.

per unit of body weight or of body surface. There was, in their opinion, no closer consistency in the caloric values when expressed per unit of body surface than when expressed per unit of body weight. In our discussion, therefore, we shall use the more convenient standard—the unit of the body weight.

Magnus-Levy [3] in 1899 studied the basal metabolism of twenty-five children of 2 years of age and upward, but the ages studied were widely scattered and the values obtained for different individuals show wide variation. For the most part his values are higher than those obtained by Benedict and Talbot.

DuBois [4] made studies of the basal metabolism of eight boys between 12 and 14 years of age. The values he obtained are also somewhat higher than those of Benedict and Talbot, but are lower than those of Magnus-Levy. Two years later he [5] studied the same boys and found that the basal metabolism per kilo had diminished but that the values obtained fell on the curve which he had deduced, using his own observations and those of others. The reduction in basal calories per kilo in case of these boys was only the normal reduction which takes place steadily with increasing years.

On the whole, it seems reasonable to accept the values for basal requirement given by Benedict and Talbot as representing what they have termed "the irreducible minimum" which must be supplied to the human organism for maintenance.

Growth Requirements.—We shall not at this point consider the special growth needs, such as necessary vitamins or the need of supplying proteins which have the essential amino-acids, but only the energy requirements for growth which are met by the fat, carbohydrate and protein furnished in the ordinary articles of food. The caloric requirements for growth must, it is obvious, be greatest when growth is most rapid and diminish at the period when growth is slower. The rate of growth is most rapid during the first year of life, diminishing greatly in the second year. It is again accelerated at the approach of puberty. The diminution in the growth rate during the early years and the acceleration during the later years is indicated by the annual increase in weight and height from birth up to the time when the body

3. Magnus-Levy and Falk: Arch. f. Anat. u. Physiol., 1899, p. 314.
4. Dubois, E. F.: Arch. Int. Med. **17**:887 (June) 1916.
5. Olmstead, W. H., Barr, D. P., and DuBois, E. F.: Arch. Int. Med. **21**:5 (Jan.) 1918.

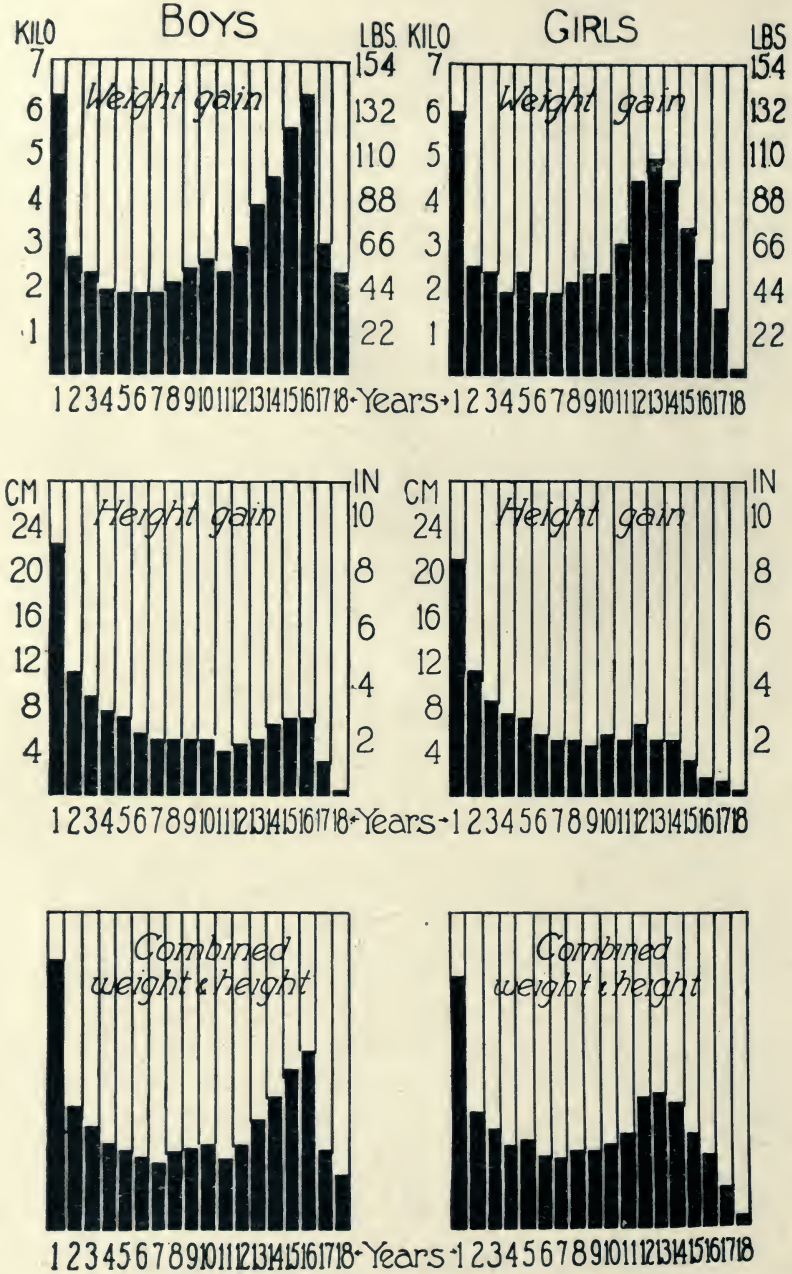

Fig. 3.—The heavy black verticals of the two upper charts show the annual gain in weight in kilos and pounds, and the gain in height in centimeters and inches, for both sexes. The lowest charts show values obtained by combining the two.

is completely grown. This average increase is shown for both sexes in Chart 3. If we combine the curve representing the annual increase in weight and that for the annual increase in height we obtain a curve which may be taken to represent the annual increase in the size of the body during the period of growth. This rate of increase steadily increases in both sexes after the age of 10. In boys by the sixteenth year and in girls by the thirteenth year it is nearly twice as great as it is at ten years.

In calculating the total caloric requirements in the past it appears that sufficient consideration has not been given to these variations in the rate of growth. The increase in the body's needs for growth is not uniform as age advances from early childhood through the period of adolescence.

Using as a basis for calculation the annual increase in weight, it is possible to estimate very approximately the number of calories needed for growth by a child at any given age and weight. Rubner [6] estimates that about 80 calories per diem are needed to increase the weight of the human body one kilo in one year. This value multiplied by the average increase in kilos per annum would give approximately the number of calories needed daily for growth. On this basis the daily caloric need for normal growth for boys is over 200 calories during the second year; between 4 and 8 years it diminishes to about 150 calories, then rises steadily, reaching over 500 calories daily during the sixteenth year, after which it rapidly falls (Chart 5).

Requirements for Muscular Activity.—It is difficult to estimate with even approximate accuracy exactly how many calories should be allowed for muscular activity. Allowance must be made for all activity, whether productive or unproductive. Even the energy expended in the process of digestion must be taken into account in estimating these needs. Benedict states that the energy needed to digest the food taken uses up about 6 per cent. of the total calories of the diet. This he terms the "cost of digestion." It is a factor not usually considered but is important. Like the food value lost in the excreta it is one of the inevitable losses and one for which allowance must be made in estimating the total caloric requirement.

The requirements of individual children for activity differ very greatly, more widely than they do in any other respect. A nervous,

6. Rubner, M.: Das Problem der Lebensdauer und seiner Beziehung zu Wachstum und Ernährung, 1908.

lively, energetic child will certainly use up more calories in activity than one of quiet, placid temperament and indolent muscular habits. How much the difference is between the actual needs of these two types we can, with our present knowledge, only conjecture.

Lusk [7] has estimated that during the period from four to fifteen years the very active child requires a little more than double the total

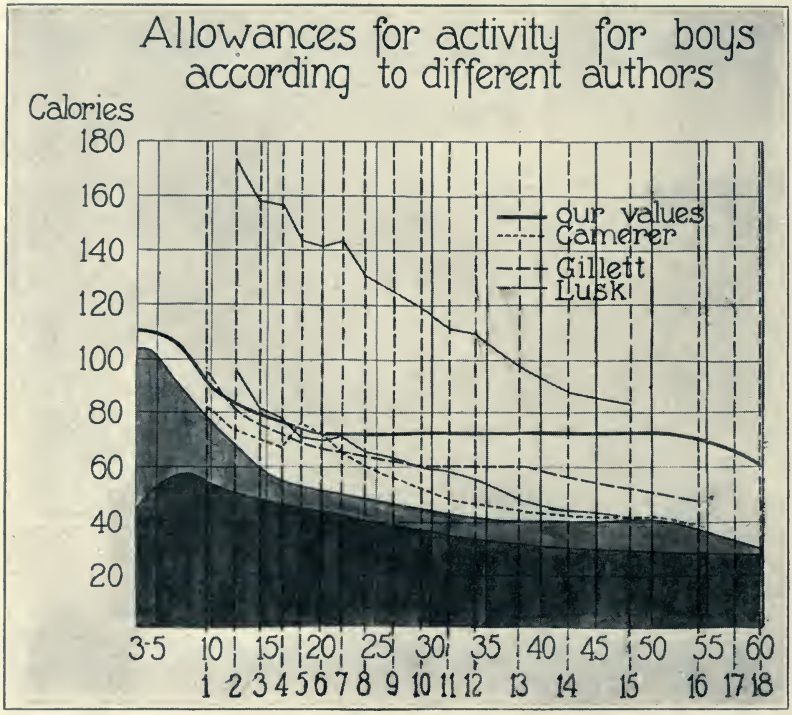

Fig. 4.—The heavily shaded area represents allowance in calories per kilo for basal metabolism; the lighter shaded area, the allowance for growth; both areas are according to our schedule. The spaces between the shaded areas and the lines above show what remains for activity according to the estimates of different authors. The solid vertical lines indicate weight; the broken lines, approximate weight at each year of age.

calories of a quiet child. Since three of the four factors which make up the total calories, namely, basal requirement, growth requirement and the food value lost in the excreta, are nearly the same for these

7. Lusk, G.: J. A. M. A. **70**:821 (March 23) 1918.

two types of children, it would appear that practically all of the increased allowance which Lusk proposes, or considerably more than half the total food taken, is used up by the very active child in muscular activity. For young children this seems excessive. It certainly cannot be taken as an average. At any age it is probably applicable only to a small group.

Lusk allows for the child of moderate activity about one-third more calories than for the quiet child. This value is probably more nearly correct for the younger children, but the allowance is not enough for boys after 12 years of age and probably not for girls.

A steady increase in the calories which are needed for activity must be allowed as age advances. As soon as a child learns to run about a great increase in activity takes place, and with the normal healthy child activity steadily increases with each year of life, at least up to the period of adolescence.

DuBois estimates that walking at a moderate pace on the level uses three times the basal requirement. On this basis, a boy of about 30 kilos weight, that is, of about 10 years of age, walking on the level for two hours, would require an increase of 270 calories to supply energy for this activity.

The great difference in food requirements of children because of the difference in their activity is not in most cases sufficiently taken into account. If the increased caloric need of the active child is not supplied by the diet, growth inevitably suffers and, as Talbot [8] has pointed out with respect to infants, there is no gain in weight. The same consequence—failure to gain weight——follows when for any reason the digestive organs are not equal to the extra task imposed by increased ingestion of food. All these factors, and not simply the average needs as worked out for large groups, must therefore be taken into account when one is considering the needs of a single child or a small group.

Food Values Lost in the Excreta.—No accurate observations on this point have been published regarding children over 6 years of age. Our own studies lead us to the opinion that this factor varies less with age than do the other three factors which make up the total food requirement, and that in health a loss of calories equal to about 10 per cent. of the food intake is approximately correct for children of all ages.

8. Talbot, F. B.: Am. J. Dis. Child. **18**:4 (July) 1919.

Some variation in children of the same age and weight will of course be seen, depending upon the amount and nature of the food, the care of preparation, on thoroughness of mastication, etc.

Extensive work done by the Department of Agriculture on the diet of adults has established quite definitely that the loss in the excreta, when a mixed diet is taken, averages about 9 per cent. of the total calories ingested. Benedict states that when a mixed diet is properly balanced and the digestion is normal, the loss in the excreta does not average more than 6 per cent. Atwater and Sherman, who followed the metabolism of three six-day bicycle riders, found an average loss in the excreta of nine per cent. of the total calories taken.

Müller[9] made a careful study of the diets of thirty-two children from 2 to 6 years of age. In order to determine the exact food value lost in the excreta, he dried the feces and urine of each child, as well as a sample of the composite food of each, and determined the exact caloric value of these substances by burning samples in a bomb calorimiter. The average caloric value of the dried feces was 5.0 calories for each gram of dried matter, the range being from 4.6 to 5.4 calories per gram. The urine showed a caloric value ranging from 8.7 to 13.9 calories for every gram of nitrogen which it contained, the average being 10.4 calories per gram of nitrogen. The average daily caloric loss in the feces of the children observed by Müller was 5.9 calories per kilo of body weight. The average loss in the urine was 4.6 calories per kilo of body weight. This gave an average total daily loss in the excreta of 10.5 calories per kilo. The average intake being 103.7 calories per kilo, the average loss in the excreta was, therefore, 10.1 per cent. of the intake. The individual loss ranged from 8 to 14 per cent. of the total caloric intake.

In our own observations we have found that healthy children under 6 years of age taking a mixed diet have from 10 to 20 gm. of dried matter in the daily stools. This represents a loss in the stools of from 50 to 100 calories, using as a basis for calculation Müller's average figure for the caloric value of dried feces. According to our observations, which confirm those of other authors, children from 1 to 6 years of age taking a mixed diet excrete from 4 to 6 gm. of nitrogen in the urine daily. Using Müller's average figure for the caloric value of urine, this indicates a loss of from 40 to 65 calories daily. The com-

9. Müller, E.: Biochem. Ztschr. **5**:143, 1907.

bined loss in urine and feces by children from 1 to 6 years of age is, therefore, from 90 to 165 calories daily. This is approximately 10 per cent. of the calories usually given at these ages, and, therefore, corresponds closely with the value suggested by Talbot for infants.

Using Müller's average caloric values for feces and urine, we have calculated the exact caloric loss through the excreta in five observations on normal children. The loss was found to range in these cases from 8.8 to 10.6 per cent. of the total calories of the food taken and the average was 9.6 per cent. We found that children suffering from a mild form of chronic intestinal indigestion had a loss through the excreta ranging from 10 to 15 per cent. of the total calories taken, while in cases of severe chronic intestinal indigestion the loss was at times as high as 25 per cent. of the total calories of the food taken. A summary of these findings is shown in Table 1.

TABLE 1.—AVERAGE NUTRITIVE VALUES LOST IN EXCRETIA

Condition of Children	Number of Observations	Age in Years	Dried Weight of Feces, Gm. Daily	Calories Lost in Feces	Nitrogen in Urine, Gm. Daily	Calories Lost in Urine	Total Calories Lost in Excreta	Calories in Food Taken	Per Cent. of Calories in Excreta	
									Aver.	Range
Normal.....	5	2-3.5	11.6	58	5.3	55	113	1,177	9.6	8.8-10.5
With mild chronic indigestion.....	10	1-3	14.5	73	4.9	51	124	1,008	12.3	10.0-14.5
With severe chronic indigestion.....	12	2.5-9*	21.1	106	5.8	60	166	865	19.2	12.9-24.7

* Some of the children in this group, although older, were much undersize and underweight and were therefore comparable to those in the other groups.

In cases of severe chronic intestinal indigestion the total food value lost in the stools must frequently be much greater than the 25 per cent. estimated. For in such cases there is usually a very large loss of carbohydrate through fermentation in the intestine. The chief products of this fermentation—gases and volatile fatty acids—do not appear in the dried matter of the stool and we have no convenient method of estimating them. Moreover, there is often some loss of protein due to putrefaction, which is represented in the stool mainly by volatile substances. How many calories these additional losses represent it is difficult to estimate.

On the whole, our estimate of 10 per cent. of the calories for loss in the excreta seems a reasonable average allowance for normal chil-

dren taking a mixed diet. This allowance would certainly be high for nursing infants, however, since our observations have shown that these infants utilize from 95 to 99 per cent. of the fat intake and a very much higher proportion of the protein intake than do artificially fed infants.

TOTAL CALORIES

A number of authors have made observations on individual children or groups of children to determine the total calories taken at different ages. A comprehensive survey of the literature on this subject up to 1917 has been made by Lucy H. Gillett.[10] In her report is given an extensive bibliography and a summary of such values reported by various authors as have been based on actual observations of food taken. Such observations are surprisingly few. Most of them have been made by the German authors and have been so widely quoted and have formed the basis of so many calculations for total calories per kilo that it seems worth while to go into detail regarding the children studied. There are objections to using the results obtained with almost all the small groups observed for the determination of the requirements of average healthy children living under normal conditions.

Hasse[11] calculated the calories taken by six girls belonging to well-to-do families. The ages of these children ranged from 2 to 11 years. All were in good health, but, as compared with our standards two were under weight, while the others were somewhat over weight. The two under-weight children, who were 2 and 5 years of age, took respectively 102 and 90 calories per kilo, rather high values for their ages. The children of 3 and 3½ years took 77 and 81 calories per kilo, about the usual for their ages. The two older girls, 9 and 11 years of age, took only 65 and 61 calories per kilo, respectively, but these girls were considerably over average weight.

Herbst[12] also observed six children in well-to-do families. Three were boys, aged 2, 4 and 10 years. The youngest was considerably over weight, the other two practically the average weight for their ages. They took respectively 90, 87 and 66 calories per kilo. The other three children were girls in their eleventh, thirteenth and fifteenth years. The first two were very much over weight, the third somewhat over weight. They took respectively 45, 41 and 38 calories per kilo.

10. Gillett, L. H.: Publication 115, N. Y. Assn. for Imp. of the Cond. Poor, 1917.
11. Hasse, S.: Ztschr. f. Biol. **18**:553, 1882.
12. Herbst, O.: Jahrb. f. Kinderh. **46**:322, 1898.

These values are very low indeed, but the children observed were in a rather exceptional physical condition and data derived from the study of their food can hardly be used as a basis for estimating the needs of the average child. These observations, however, confirm the generally accepted opinion that the food requirements per kilo of overweight children are much lower than those of children of average weight for their age.

Müller [9] studied twenty-three boys and nine girls, each for a six-day period, and collected and analyzed the urine and feces of each child, as well as recording the exact amount and kind of food taken. The ages of the children ranged from 2 to 6 years. The children were reported to be healthy and free from nutritional disturbances, but all were inmates of an orphan asylum and appear to have been fair examples of what is commonly spoken of as "institution children." Nearly all of the children were under weight, the boys almost without exception markedly so. As might have been expected with children of this class, the intake per kilo was high, the average for the group being 104 calories per kilo. Two-thirds of the boys weighed between 11 and 15 kilos and these boys, all under weight, took on the average 113 calories per kilo. One boy of 4 years with the weight (12.6 kilos) of an average child of about 2 years, took 132 calories per kilo; another child, 6 years old, of about the same weight as the one just mentioned, took 126 calories per kilo.

The girls, who were not so much under weight as the boys, took on the average about 15 calories per kilo less than did the boys. These values correspond fairly well with the usually accepted ones for their ages, except in the single instance of one girl who was about the average weight for her age and who took only 71 calories per kilo.

Müller's observations were made in winter. He thinks that season should be taken into account in estimating the food needs. His results show that children who are much below normal weight require much more food per kilo than do normal children. All the facts concerning the children observed must be known in order to appreciate and properly interpret the data obtained. We are no more justified in basing our estimates for normal requirements upon the results obtained with these underweight children than on the results with Herbst's overweight girls.

Uffelmann [13] made observations on his own children, all boys, at the age of 2, 4, 10 and 15 years. The oldest and youngest were somewhat, the other two very much under weight. Contrary to general experience, the calories per kilo reported to be taken by these children were low. We can hardly resist the inference that, if the diet at the time of observation was typical of that usually taken, these children were below weight because underfed.

Camerer [14] made extensive observations of the amount of food taken by his own children, four girls and one boy, at different times extending over a period of years. In the observations made at ages under 7 years the calories per kilo taken by both sexes were about the usual for those ages. In the later observations, however, the calories per kilo were very low and diminished rapidly with increasing age, so that in the observations made at ages over 15 years the calories per kilo taken by both sexes were only a little above the basal requirements as determined by Benedict and Talbot. Camerer's girls were on the average much below the average weight for age at the time of observation and during the early years the boy was somewhat under weight. Accordingly a high caloric intake would have been expected. The fact that, on the contrary, the calories per kilo taken by these children were very low suggests, as we have said in regard to Uffelmann's children, that the under weight was possibly due to under feeding.

Baginsky [15] has given values obtained from a study of a number of children convalescent from various forms of acute disease and with one exception much under weight. As might be anticipated, his values are for the most part high.

E. H. Starling,[16] quotes Carl Tigerstedt, who made forty-seven observations on children ranging from 4 to 14 years of age. The weights unfortunately are not given, only the calories per kilo. The striking thing in these observations is the wide range of calories taken. For example, in four observations on children in their fifth year the range was from 73 to 114 kilos; in five observations for the seventh year, from 71 to 102; nine observations for the twelfth year, from 44 to 89; seven observations for the fourteenth year, from 43 to 82

13. Uffelmann, J.: Hygiene des Kindes, 1881.
14. Camerer: Stoffwechsel des Kindes, 1896.
15. Baginsky, A.: Arch. f. Kinderh. **23**:119, 1897, and **16**:398, 1893.
16. Starling, E. H.: The Feeding of Nations, 1919.

calories per kilo. Starling calls attention to the dangers involved in basing estimates for food requirements on averages, especially when these include only a small number of observations.

In marked contrast to the values found by most of the authors mentioned above are those of Gephart,[17] whose observations were made in quite a different manner. His method was that employed by other writers in studying the actual amount of food consumed by soldiers in camps, and seems to be a reliable way of determining the average number of calories taken. Gephart studied the diet of about 350 boys in a large boarding school (St. Paul's, Concord, N. H). in the following manner: He first calculated the caloric value of the entire amount of food purchased during the period of observation, the entire school year. From this he subtracted the values obtained by analyzing at various times the garbage and the waste. The remainder he divided by the total number of meals served, and thus obtained an average caloric value per meal for the school. In addition to the meals which were provided by the school, the boys were accustomed to buy from a confectioner's shop considerable extra nourishment—sweets, chocolate, cakes, etc. The total amount purchased during the period was known and was apportioned by Gephart among the boys of the whole school. The calories furnished by this additional food were found to be about one-eighth of the total daily consumption.

TABLE 2.—SUMMARY OF GEPHART'S OBSERVATIONS ON BOYS AT ST. PAUL'S SCHOOL

School	Average Age in Years	Average Weight		Average Calories per Kilo			Average Total Daily Calories
		Kilos	Pounds	School	Food Shop	Total	
Lower	13.5	43.6	96	98	15	113	4,949
Middle	14.5	50.8	112	88	13	101	5,126
Upper	16.1	60.6	133	71	11	82	4,997

The average daily caloric intake was found to be about 5,000 calories per boy, and all but the group of the oldest boys took over 100 calories per kilo. The boys were divided into three groups, the lower, the middle and the upper school. In Table 2 are given the ages, average net weight, calories per kilo furnished by the school, additional calories purchased at the confectioner's, average total calories per kilo and average daily total calories for each group.

17. Gephart, F. C.: Boston M. & S. J. **176**:17, 1917.

While the conclusions which might be drawn from these observations may perhaps be open to question, still, the results show what amount of food is actually taken by the average American school boy at the ages studied, under the special conditions represented by these observations. It may be argued that these conditions were not average but somewhat exceptional. The boys were living in a rigorous climate; they were taking a great deal of active out-of-door exercise and they were at an age when growth is most rapid. Furthermore, the well-known disposition of boys of these ages to stuff themselves with food apparently beyond their actual needs must also be taken into account. Still when due allowance has been made for all these conditions, the fact remains that the enormous appetite of active, growing boys represents a physiological need which in the past has not been given sufficient consideration.

Studies made on such large groups are likely to give results much nearer the truth than observations made on a few individuals or the children of one family, no matter how carefully these observations have been made. The results of the German observations which we have quoted would lead one to allow too little food for children during the active growing period.

The Department of Agriculture has made many observations on the amount of food taken by families, including children, but has not determined experimentally what proportion of the food was taken by each child. They have apportioned the diets theoretically according to a commonly used system of coefficients; for example, assuming that if a man takes one portion, a woman takes 0.8, a boy of 12 takes 0.8, a boy of 8 takes 0.7, etc.

Schedules Proposed by Various Authors.—Several authors have proposed complete schedules of theoretic caloric requirements from infancy to adult life. These have been based either on their own observations or on those of others. Most of these observations we have just discussed.

Among the German observers, Camerer's schedule has been most often quoted as a standard. His suggested allowance for boys is 89 calories per kilo at the age of one year and diminishes to 75 calories at 4 years. For the age of 5 years the allowance is increased to 84 calories. From that age the allowance decreases rapidly and steadily

to adult life. His values after 6 years are low, and after 9 years extremely so. After the twelfth year his allowance is but little above the basal requirements as shown by Benedict and Talbot.

Steffen [18] offers a schedule for children up to six years of age and allows over 100 calories per kilo through this entire period.

Uffelmann has proposed a schedule for the first five years of life. His values are rather low, ranging from 88 calories per kilo at one year to 68 calories at five years.

Gillett and Sherman, after giving due consideration to the observations which have been published and which are summarized by Gillett, present a table of suggested values for total daily calories for children of both sexes throughout the entire period of growth. They allow a considerable range of variation. Their allowance diminishes gradually to 68 calories per kilo at 9 years and is maintained at that figure up to the age of 13, dropping to 65 at 14 years. After this age the average allowance is rapidly decreased to 55 calories per kilo at 16 years. This decrease in calories per kilo during the period of most rapid growth after the age of 13 seems to us injudicious.

Lusk has recently published estimates for total calories. As already mentioned, he makes a very large allowance for activity and gives three curves—for the quiet child, the active child and the very active child. He allows the same percentage increase in total calories for increased activity, quite irrespective of age and weight. That is, his values for the active child are about one and one-third times those for the quiet child at all ages, while the values for the very active child are about twice those for the quiet child at all ages. Accordingly, his estimates for total calories for the very active child and even for the child of moderate activity, are extraordinarily high for the early years, for example, 193 and 129 calories per kilo, respectively, for a boy of 2 years. The diminution in calories per kilo with increasing years is rapid according to all three of his curves. His values for the quiet child after the age of 13 are very little above the calories necessary for basal metabolism and for normal growth. No allowance is left for activity, which of course can never be reduced to zero.

Gillett and Sherman and also Camerer give schedules for girls as well as for boys. According to both the allowance for girls is

18. Steffen, W.: Jahrb. f. Kinderh. **46**:332, 1898.

considerably lower than that for boys, and from the twelfth year the allowance exceeds only by very little the needs for basal metabolism and growth.

PROPOSED SCHEDULES FOR CALORIES PER KILO

In the light of our own observations and those of others, the theoretical schedules for calories per kilo of body weight shown in Charts 1 and 2 and Tables 3 and 4 are suggested. The charts show the curves and the tables the actual figures, on which the curves are based, for the different factors which make up the total calories per kilo. The tables show also the percentage allowance for each of the different factors.

TABLE 3.—SUGGESTED CALORIES PER KILO FOR BOYS

Weight, Kilos	Calories per Kilo					Per Cent. of Calories for				Total Calories Daily
	Basal	Growth	Activity	Excreta	Total	Basal	Growth	Activity	Excreta	
3	46	56	8	10	120	38	47	7	8	360
4	50	52	8	10	120	42	43	7	8	480
5	54	46	8	10	118	46	39	7	8	590
6	56	38	10	10	114	49	33	9	9	685
7	57	32	11	10	110	52	29	10	9	770
8	56	28	12	10	106	53	26	11	10	850
9	55	25	12	10	102	54	24	12	10	920
10	54	22	13	10	99	55	22	13	10	990
11	53	19	14	10	96	55	20	15	10	1,060
12	52	16	16	9	93	56	17	17	10	1,120
13	51	14	17	9	91	56	16	18	10	1,180
14	50	13	17	9	89	56	15	19	10	1,240
15	49	12	17	9	87	56	14	20	10	1,300
16	48	10	18	9	85	56	12	22	10	1,360
17	47	9	19	8	83	56	11	23	10	1,410
18	46	8	20	8	82	56	10	24	10	1,470
19	45	7	21	8	81	56	9	25	10	1,540
20	44	7	21	8	80	55	9	26	10	1,600
22	42	7	23	8	80	53	9	28	10	1,760
24	41	8	23	8	80	51	10	29	10	1,920
26	39	8	25	8	80	49	8	31	10	2,080
28	38	7	27	8	80	47	9	34	10	2,240
30	36	7	29	8	80	45	9	36	10	2,400
33	35	7	30	8	80	44	9	37	10	2,640
36	33	8	31	8	80	41	10	39	10	2,880
39	32	9	31	8	80	40	11	39	10	3,120
42	31	10	31	8	80	39	12	39	10	3,360
45	30	11	31	8	80	38	13	39	10	3,600
48	30	11	31	8	80	38	13	39	10	3,840
51	29	11	31	8	79	38	13	39	10	4,030
54	29	8	31	8	76	38	11	41	10	4,100
57	28	5	30	7	70	40	7	43	11	3,990
60	27	2	27	7	62	43	3	44	10	3,720
68 (Adult)	25	0	18	5	48	52	0	38	10	3,265

The basal requirement adopted is that of Benedict and Talbot. This, it will be seen, after reaching a maximum at about the ninth month, falls steadily through the entire period of growth to adult

life. The basal requirement per kilo for girls is lower than that for boys up to the age of 11 years, after which it is higher than that for boys until the completion of growth.

The growth allowance has been calculated from the average normal rate of growth, which has been well established. The calories allowed for growth fall steadily from the first year to the sixth year, then remain practically constant up to eleven years for girls and thirteen years for boys, when a marked increase takes place. This increased need is evident for about three years with both sexes, after which the growth needs rapidly diminish to zero.

TABLE 4.—SUGGESTED CALORIES PER KILO FOR GIRLS

Weight, Kilos	Calories per Kilo					Per Cent. of Calories for				Total Calories Daily
	Basal	Growth	Activity	Excreta	Total	Basal	Growth	Activity	Excreta	
3	51	51	8	10	120	43	43	6	8	360
4	53	49	8	10	120	45	41	6	8	480
5	55	45	8	10	118	47	38	7	8	590
6	56	38	10	10	114	49	33	9	9	685
7	56	33	11	10	110	51	30	10	9	770
8	57	27	12	10	106	54	25	11	10	850
9	56	24	12	10	102	55	23	12	10	920
10	55	21	13	10	99	56	21	13	10	990
11	53	19	14	10	96	55	20	15	10	1,060
12	51	17	16	9	93	55	18	17	10	1,120
13	49	16	16	9	90	54	18	18	10	1,170
14	47	14	17	9	87	54	16	20	10	1,220
15	45	12	19	8	84	54	14	22	10	1,260
16	44	11	19	8	82	54	13	23	10	1,310
17	43	10	19	8	80	54	12	24	10	1,360
18	42	9	19	8	78	54	12	24	10	1,400
19	41	8	20	8	77	53	11	26	10	1,460
20	40	7	21	8	76	53	9	28	10	1,520
22	38	8	22	8	76	50	11	29	10	1,670
24	37	8	23	8	76	49	11	30	10	1,820
26	36	8	24	8	76	48	10	32	10	1,980
28	36	8	25	8	77	47	10	33	10	2,155
30	36	9	26	8	79	46	11	33	10	2.370
33	35	10	27	8	80	44	12	34	10	2,640
36	35	10	27	8	80	44	12	34	10	2,880
39	35	10	27	8	80	44	12	34	10	3,120
42	34	9	27	8	78	44	11	35	10	3,275
45	34	7	26	7	74	46	9	35	10	3,330
48	33	5	22	7	67	49	8	33	10	3,215
51	32	3	21	6	62	51	5	34	10	3,160
54	31	0	18	5	54	57	0	33	10	2,915
60 (Adult)	25	0	15	4	44	57	0	33	10	2,640

The needs for basal metabolism and for growth, though subject to considerable individual variation, are, as averages, practically irreducible.

The allowance for activity is admitted to be hypothetical. For reasons previously given, this has been increased steadily from the second to the thirteenth year for boys and to the twelfth year for

girls. Whether the allowance for activity should be further increased during the period of most rapid growth (in girls from the twelfth to the fourteenth or fifteenth year and in boys from the thirteenth to the seventeenth) is somewhat doubtful. It is a matter of common observation that while the body is increasing so rapidly in size as it does at this time, "the lazy age," there is frequently seen in both sexes a growing disinclination to active muscular exertion, which is usually accompanied by a corresponding disinclination to mental activity, sometimes amounting almost to mental lethargy. A very considerable stimulus may be needed to voluntary effort, both mental and physical. This is not surprising; it is rather to be expected and may be considered physiologic. The opinion is not only an impression from our own observations but is confirmed by the head masters and athletic directors of six large schools for boys with whom we have discussed the question. For the reasons above given we have felt that no increase in the caloric allowance per kilo for activity should be made during these years of most active growth; possibly even a slight reduction should be considered.

The number of calories we have allowed for loss in the excreta is 10 per cent. of the total after the first year of life, during which period a somewhat smaller proportion should be allowed, certainly for nursing infants.

With the values proposed for the different factors just discussed the total calories per kilo are for both sexes about 120 during the early part of the first year, diminishing to 100 at one year, and reaching 93 calories per kilo at 2 years. After the second year there is an appreciable difference between the total calories per kilo allowed for boys and for girls, owing largely to the difference in their basal requirement, that of girls being, from this time until the end of the tenth year, several calories lower than that of boys. The calories per kilo allowed for both sexes slowly fall, largely because of the slowing up of the growth rate. We have estimated that at 6 years the total for boys should be 80 calories per kilo and for girls 76 calories per kilo. For girls the calories per kilo have been increased from 76 to 80 during the eleventh year, since there is at this time an increased growth need and since the basal needs for this and the next few years are nearly uniform. This higher value is continued for girls to about the fourteenth year. After the sixteenth year in boys and the four-

teenth year in girls, since there is a rapid decline in growth needs and possibly some reduction in activity, the total calories per kilo have been rapidly reduced to adult standard—about 48 for males and 44 for females.

The chief difference between our schedule for total calories per kilo and others which have been proposed, is that in our schedule the total calories per kilo are nearly uniform from the age of six to the end of the period of rapid growth.

In the practical application of these suggested values it must be borne in mind that each component part of the caloric requirement is subject to considerable individual variation. The curve suggested aims only to give averages. The calories actually given must vary to fit the individual needs. Activity is of course the most obvious variant. An extremely active child will undoubtedly utilize more calories than the average which we have allowed, while the needs of a quiet child may be supplied by somewhat less than our suggested values.

Another cause for variation in the caloric requirement for the individual is the relation of weight to height and age. Our observations and those of others show that the underweight child will take and utilize more calories per kilo than the child of average weight; while, as might be expected, one who is overweight does not take and does not need the average number of calories per kilo. The fact must be taken into account in making the caloric allowance for an individual child.

It seems reasonable to allow for the younger children a normal range of five calories per kilo above and below the average given, and to allow the older children a range of eight to ten calories above and below the average. For instance, the normal range allowed for a boy of 2 years might be from 88 to 98 calories per kilo, for a boy of six from 72 to 88 calories and for one of 15 a range from 70 to 90 calories per kilo. When activity is excessive, however, an increase of 20 or even 30 calories above the average may be well utilized.

Comparison of Schedules Proposed.—In order to show the difference between our suggested schedule for calories per kilo and others which have been proposed, Table 5 and Chart 4 are given. The table shows the calories per kilo proposed by various authors for both boys and girls at different ages. This table brings out clearly the points already mentioned in discussing the schedules offered. The only

schedule which allows more calories per kilo throughout the entire range of years than does ours is that of Lusk for the very active child. During the early years this schedule shows about twice as many calories per kilo as we have considered sufficient. The difference diminishes after the age of seven, until at the age of fifteen his values are but little above ours. Lusk's estimate for the child of moderate activity exceeds ours up to the age of twelve, after which his values fall considerably below ours. The other complete schedules, those of Gillett and Camerer, are much below ours after the age of seven or eight. The two schedules for girls show values very much below ours after the age of six years.

TABLE 5.—COMPARISON OF SCHEDULES FOR TOTAL CALORIES PER KILO

Author	Age, Years															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Boys:																
Holt and Fales	100	93	88	84	82	80	80	80	80	80	80	80	80	80	80	75
Gillett	105	90	83	79	77	75	73	71	68	67	68	69	68	65	60	55
Lusk, quiet child	79	97	90	88	79	78	79	73	70	66	66	62	54	48	45	
Lusk, active child	...	129	117	116	105	105	105	97	93	88	83	82	73	66	62	
Lusk, very active child	...	193	177	175	158	158	159	146	139	132	124	123	109	98	93	
Camerer	89	80	78	75	84	77	72	67	63	58	55	52	49	47	45	42
Uffelmann	88	80	73	71	68											
Steffen	113	99	105	125	114	103										
Girls:																
Holt and Fales	101	94	87	82	78	76	76	76	76	77	80	80	79	74	67	62
Gillett	105	93	83	79	73	71	69	66	64	62	59	55	51	48	47	46
Camerer	89	80	78	75	70	67	64	62	60	58	55	51	47	43	41	39

On Chart 4 the basal metabolism and the growth needs are indicated by the heavily and lightly shaded areas respectively. As we have said, these are, as averages, practically irreducible. The various curves shown in the chart were obtained by plotting the values offered in the various schedules after subtracting the ten per cent. of the total calories which is lost in the excreta. Therefore, the space between the shaded areas and the various lines represents the allowance for activity according to the different authors. The great difference is at once apparent. The curves representing total calories per kilo would be obtained by raising each of the curves shown by the addition to the values plotted of the ten per cent. allowance for loss in the excreta.

The curve based on Camerer's values shows very little allowance for activity except between the ages of 4 and 8 years and after the age of 13 years practically none at all.

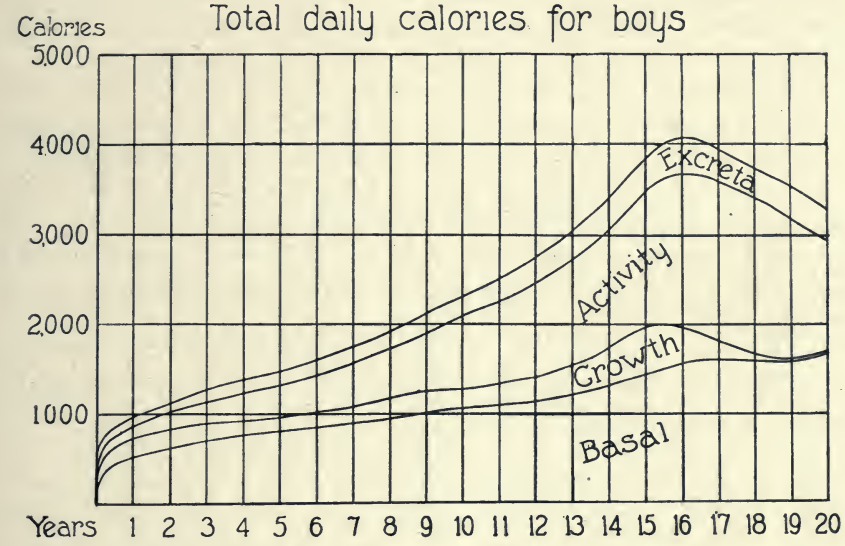

Fig. 5.—The distance between the base and the upper line shows the allowance for total daily calories according to age, from birth to adult life. The spaces between the various lines, from the base line upward, indicate the allowance for the different factors which make up the total, namely, for basal requirement, growth, activity and loss in excreta.

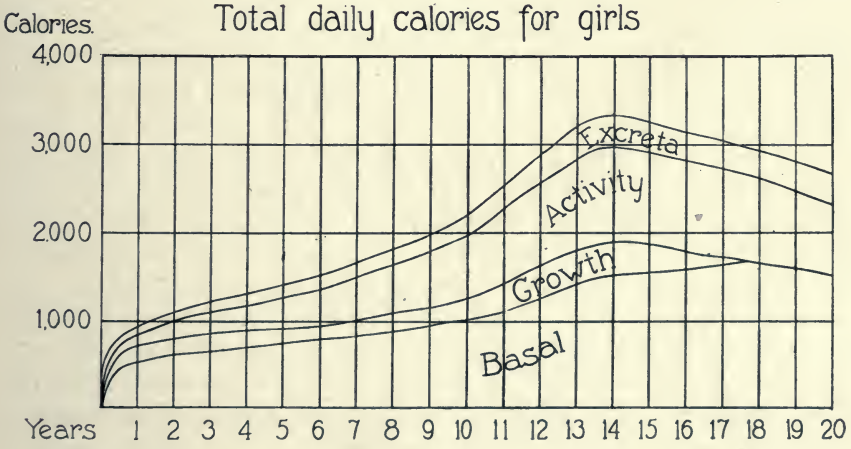

Fig. 6.—The curved lines and spaces have the same significance as in Chart 5.

The curve based on the average values offered by Gillett and Sherman does not differ greatly from our own up to the age of 7 years. From 7 to 14 years it is nearly parallel with ours, but somewhat lower. After 14 years their curve falls rapidly. In our judgment they have allowed far too little for activity and growth during adolescence. As previously stated, they allow a fairly wide individual variation in total calories, but even if their maximum allowance is taken, the calories per kilo after the age of 14 are only about five calories higher than the values shown on the chart, and therefore, still about fifteen calories per kilo lower than the values we have suggested.

The curve based on Lusk's values for the quiet child is almost identical with our own from 2 to 7 years. After this age his allowance for activity diminishes very rapidly and becomes practically zero at fourteen years. He gives a schedule, not represented here, for the child of moderate activity which, when plotted, is represented by a curve almost parallel to the one just discussed but about one-third higher. His curve for the very active child seems to give an extreme allowance for activity, certainly for the first ten or twelve years of life. At the age of 15 his allowance is not far above our own.

Total Daily Calories.—Charts 5 and 6 and Table 6 gives for boys and girls the average values for total daily calories based upon the values for calories per kilo just proposed by us. The curves shown on the chart are plotted on the basis of years of age, using the average normal weights at the different ages. The charts show not only the total daily calories but also the components—basal needs, growth needs, allowance for activity and for loss in the excreta—which together make up the total.

The daily calories allowed for the boys and girls are about 950 at one year. They increase with succeeding years for both sexes, the increase for the boys being a little more rapid than for the girls until the age of 12 is reached. From 12 to 14 the total calories for the girls exceed those for boys. After fourteen, the allowance for boys is considerably greater than that for girls. The highest values for daily calories are 3,330 for girls at the age of 14 and 4,100 for boys, at the age of 16. After these maximum figures are reached the values drop very rapidly to adult standards for moderate activity,—about 2,640 for women and 3,265 for men.

These charts show the provision for the increase in the growth needs during the period of adolescence. The growth need, calculated

according to Rubner's formula, reaches for girls 380 calories daily during the thirteenth year, and for boys about 500 calories daily during the sixteenth year. It is this greatly increased need of calories for normal growth at this period that has not been sufficiently taken into account by many authors in estimating the total daily calories required by the growing child.

TABLE 6.—SUGGESTED TOTAL DAILY CALORIES

Age Years	Boys					Girls				
	Average Weight		Calories per		Total Daily Calories	Average Weight		Calories per		Total Daily Calories
	Kilos	Pounds	Kilo	Pound		Kilos	Pounds	Kilo	Pound	
1	9.5	22	100	45	950	9.3	21	101	45	940
2	12.2	27	93	42	1,135	11.8	26	94	43	1,110
3	14.5	32	88	40	1,275	14.1	31	87	40	1,230
4	16.4	36	84	38	1,380	15.9	35	82	37	1,300
5	18.2	40	82	37	1,490	18.2	40	78	36	1,410
6	20.0	44	80	36	1,600	20.0	44	76	34	1,520
7	21.8	48	80	36	1,745	21.8	48	76	34	1,660
8	24.0	53	80	36	1,920	23.9	53	76	34	1,815
9	26.4	58	80	36	2,110	26.2	58	76	34	1,990
10	29.1	64	80	36	2,330	28.5	63	77	35	2,195
11	31.4	69	80	36	2,510	31.5	69	80	36	2,520
12	34.2	75	80	36	2,735	35.8	79	80	36	2,864
13	38.0	84	80	36	3,040	40.6	89	79	36	3,210
14	42.5	94	80	36	3,400	45.0	99	74	34	3,330
15	48.2	106	80	36	3,855	48.3	106	67	30	3,235
16	54.5	120	75	34	4,090	51.0	112	62	28	3,160
17	57.5	127	69	31	3,945	52.6	116	58	26	3,060
18	59.8	132	62	28	3,730	52.8	117	56	25	2,950
Adult	68.0	150	48	22	3,265	60.0	132	44	20	2,640

The large allowance for activity is of course the most debatable factor in our estimate. Some may think that this allowance is excessive but the more recent observations, particularly those of Gephart, seem to justify our position. Our values for the total daily caloric allowance for boys of the age of those studied by Gephart are still much below the calories which he found to be actually taken by the boys he observed. However, as we have stated, these boys were living under rather exceptional conditions and the calories taken by them can hardly be used as a basis for estimating normal averages.

According to our schedule the allowance for activity varies from 6 per cent. of the total calories during the first year to a maximum of 44 per cent. of the total calories during the period of adolescence. This does not seem excessive for this active period.

It is a common observation and an undoubtedly true one, that during adolescence the average boy or girl takes more food than the average adult man or woman. Unquestionably, this represents a real

physiologic need. It is only by assuming such values for calories per kilo as we have proposed that one can reach a total daily caloric intake which will be in accord with these conditions.

The several authors who have given complete schedules for food requirements steadily increase the total daily calories with age through childhood and adolescence up to the standard allowance for adults. No one has up to the present proposed a schedule according to which the values for total daily calories exceed adult standards during adolescence and drop to adult standards with the completion of growth. This seems to us to be absolutely necessary. Unless this is done, the increasing growth needs must be deducted from the allowance for activity, leaving for the latter a very small remainder; or, on the other hand, if activity is maintained, growth must suffer. The modern child, boy or girl, is usually an active person during adolescence. If in school, he is required by school routine to take systematic exercise. If he has left school and entered industrial life he may be continually compelled to expend physical energy. In view of these facts it is evident that the food taken by perhaps the majority of boys of the poorer classes who are engaged in active industrial occupations during this period of rapid growth, is totally inadequate. An arrest of growth is the almost inevitable consequence of forced activity on a limited ration.

ORIGINAL OBSERVATIONS

Because there have been so few observations reported in the literature which give the calories taken by normal children under average conditions and because of the objections, already discussed, to drawing conclusions from a small number of observations, we have endeavored to collect a sufficient number of individual diet records to warrant some conclusions. This has proven to be a laborious and difficult task. We have at present, however, obtained dietary records from over one hundred selected children of both sexes from 1 to 16 years of age, who were healthy, well cared for, and normal as to digestion. They were almost all children in private families, living in excellent surroundings. The parents were intelligent people, interested in the purpose of our experiment, and willing to cooperate. The children were supposedly intelligently fed and it can be assumed that they were receiving diets fairly typical of those usually taken by well children.

A report of the net weight, height, activity, appetite, general condition, etc., was obtained, together with a record of the exact amount

of each item of food taken by the child for four consecutive days. From these data the caloric value of the average daily diet was calculated. Not only was the value for the total calories obtained, but also the distribution of the calories as fat, carbohydrate and protein, which, together with other facts brought out, will be discussed in succeeding papers. Established caloric values of the common articles of food have been compiled in a convenient form by Locke.[19] These have been for the most part used. Other authors whose publications we have found valuable for reference in this study are Leach,[20] Sherman,[21] Lusk [22] and Jordan.[23] The values of a number of articles were calculated from the results of analyses made in our own laboratory.

This method of estimating the calories taken by children is of course not absolutely accurate but it undoubtedly gives a very close approximation. While there are slight variations from the usual caloric values of the food taken owing to differences in the methods of preparing food, it is probable that these errors tend to balance each other and that the net result is approximately accurate. We feel certain that in no case did the child receive less food than was reported. It is not unlikely that in some cases a child actually took more food than was reported, especially the older children whose diet is not so carefully supervised and who are more likely to eat between meals without the knowledge of the parent. If there is, therefore, an appreciable error in the estimation of the calories, it is that the calculated amount is somewhat low.

The largest number of the records were of children under 11 years of age. There are from five to twelve observations for each year up to the age of 11. Beyond this age the number of observations for each year is too small to warrant definite conclusions.

In Chart 7 are shown the total calories taken by these children arranged according to age. The curves shown are those based upon the schedules proposed by us for average daily calories at different ages. The curve for boys is indicated by the solid line, that for girls by the broken line. The individual observations for boys are shown by the dots, those for girls by circles.

19. Locke, E. A.: Food Values, 1917.
20. Leach, A. E.: Food Inspection and Analysis, 1920.
21. Sherman, H. C.: Chemistry of Food and Nutrition, 1919.
22. Lusk, G.: The Science of Nutrition, 1919.
23. Jordan, W. H.: The Principles of Human Nutrition, 1919.

This chart shows, as was to be expected, a wide variation in individual observations. However, the observations mostly fall near the curves and up to the age of 11 the average would fall very near the curves. Beyond that age there are as yet too few observations to be conclusive. However, those made on older boys are very close to the proposed curve.

Some of the observations which vary most widely from the average curves deserve special mention. There were eight children in the series whose total calories taken amounted to over one-third more than the theoretical average requirement, but every one of these children was

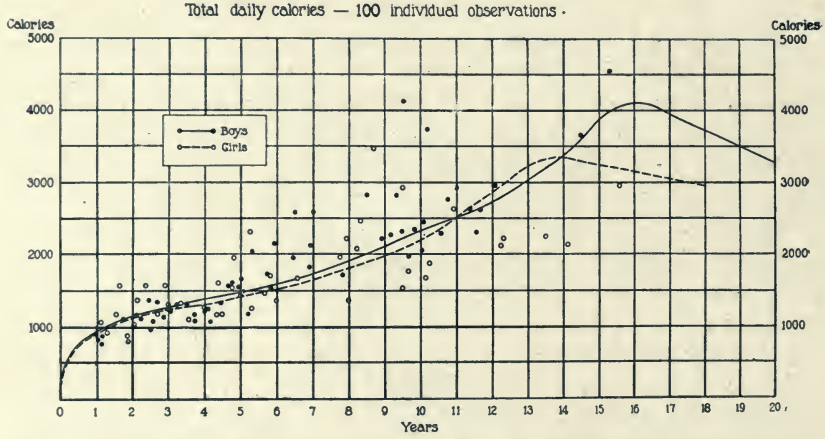

Fig. 7.—Curved lines represent suggested total daily calories according to age, the solid line the curve for boys, the broken line for girls. The dots represent the calories taken in individual observations on boys, the circles those taken by girls.

reported to be exceedingly active. There were only two children, both girls, whose total calories were more than one-third less than the theoretical average requirement, but these girls were both very large for their ages, in fact, had nearly attained adult stature and accordingly did not need the number of calories for growth usual for that age.

On the whole, it would seem that the curves suggested are approximately correct for the average caloric requirements up to the age of 11 years. We feel confident that a larger number of observations for the later years will verify the estimates for those years also.

When the individual observations are considered on a per kilo basis and compared with the proposed curves for calories per kilo, the individual observations show wide variation, but practically all the high values for calories per kilo were found in case of very active children or those who were very much under weight for their height or undersize for their age. The values which were found to be much lower than the average shown by the curves were mostly in case of quiet children or those who were either large for their age or over weight for their height.

SUMMARY

1. In calculating the total caloric requirements of children there must be considered separately the component parts of which the total is made up. These are the requirements for basal metabolism, for growth, for muscular activity and the food values lost in the excreta.

2. The basal requirements, which have been determined by Benedict and Talbot, are highest per kilo at about nine months and steadily fall from this time up to adult life.

3. The food value normally lost in the excreta is a nearly uniform proportion of the intake, about 10 per cent., for all ages after infancy.

4. The requirements for growth are greatest during the period when growth is most active, namely, during the first year of life and during adolescence. They are nearly uniform from the fourth to the tenth or eleventh years.

5. The average for three factors—basal, growth requirements and food values lost in excreta—are nearly uniform for children of the same weight living under similar conditions.

6. The requirement for activity is the only factor which varies widely with different individuals.

7. The great differences in the calculations of different writers who have estimated theoretical values for total calories per kilo for children are in part due to the fact that they have not sufficiently considered the different component parts which make up the total.

8. The average caloric requirement of children according to our observations is about 100 calories per kilo at an age of 1 year (about 9.5 kilos). For boys it falls to about 80 calories at 6 years (about 20 kilos) and remains practically constant at this value up to the age of 15 years, the increasing requirements for activity being met by the

reduction in basal requirements per kilo. After a weight of 50 kilos (about 15 years), is reached the calories per kilo can rapidly be reduced to adult standards, about 48 calories per kilo. The requirement for girls falls to 76 calories per kilo at 6 years (about 20 kilos), continues at this value until the tenth year. During the tenth year it rises because the basal requirement is nearly constant while there is an increase in needs for growth and activity. The requirement remains at 80 calories per kilo until growth is complete, then falls rapidly to adult standards, about 44 calories per kilo.

9. In our calculation we have allowed a much higher value for calories per kilo during adolescence than have others. This seems to be absolutely essential, because of the increased growth needs at this time and the large requirement for muscular activity.

10. According to our allowance the total daily caloric requirement of children of both sexes during adolescence exceeds by nearly 1,000 calories the requirements of the adult man or woman of moderate activity.

11. Children who are under weight require more calories per kilo than those who are of average weight for their age. Children who are over weight require fewer calories per kilo than those of average weight.

12. The schedule here proposed is a tentative one and is based on present knowledge, which is in many respects incomplete. There are a number of points which must be studied more fully before definite standards can be established.

For the many reasons which we have discussed, it seems the right procedure to allow for children during the period of adolescence more calories than the adult ration and, as growth needs end, to diminish the caloric allowance to the adult standard. We quite agree with Benedict's recent statement, "It is still, however, the best practice to give a most liberal diet to children, since the greater part of the evidence on under weight indicates that children usually receive too little rather than too much food."

DISCUSSION

DR. PISEK: Dr. Holt has a happy faculty of recognizing our needs and meeting them. We have needed to know more about the nutritional requirements of the child after the first year of life. It is a particular satisfaction that he has made these estimations on the basal curve and that this has been plotted by a man in our association. I was particularly interested in

seeing how he worked out the curve of activity. We all feel that this is a personal equation, one that we must work out in trying to feed a child. He has made it possible to strike a ready average and make a ready calculation of that factor. As to total calories, 4,000 may seem high but it will not seem so high if one thinks of the pathological cases, and the type of cases that need to be fattened up. With these children we do not expect to have any difficulty on an increased ration if it is well balanced. I am glad we have these figures to guide us.

DR. TALBOT: Dr. Holt has covered the subject so completely that he has left little to be said regarding the nutritional requirements of children from the age of 1 year to puberty. What Dr. Holt says about the total number of calories required by the child per kilo applies also to the basal metabolism. The under weight child requires much more food as his basal metabolism per unit of body weight is higher. The fatter the child is the lower is his basal metabolism. The same holds true of the normal. The normal variation is about 10 per cent. but we must have an average line. I assume from what Dr. Holt says that this represents what the average normal child may eat and not what the individual child must eat. As to activity I can make two very definite statements. We found that the basal metabolism of two infants was increased 100 per cent. when quiet as compared with a convulsion, so you can see to what extent activity will increase the caloric needs of a given child.

DR. SMITH: This paper illustrates the increasing emphasis placed on the care of the well child. We have been devoting ourselves for a long time to the ill child, and only a small proportion of the children we see are ill. We have neglected the children who are well, who really constitute the average children. We have here an indication for the feeding of children which represents a very important part of our work.

DR. HOOBLER: This paper gives a foundation for feeding children at the age of 3 or 4 years, the age at which it has been most difficult to map out a course of feeding. I agree with Dr. Talbot that as you increase the activity of these children their metabolism is increased. Murlin and I did some work which showed that during activity the metabolism was regularly increased about 60 per cent. above the basal metabolism. Dubois has reported on boys 13 and 14 years of age, in connection with the work of the Sage Foundation. His results were in keeping with the marked increase in metabolism just preceding puberty shown in Dr. Holt's charts. I am much interested in the mixed diets passed out to the families.

THE ULCERATED MEATUS IN THE CIRCUMCISED CHILD

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For a number of years my attention has been drawn with increasing frequency to a peculiar lesion of the meatus urinarius occurring only in circumcised male children, and characterized by ulceration, crusting, narrowing of the urinary passage, and nearly always accompanied by painful urination, often with distended bladder, and, occasionally, by hemorrhages. I have been able to find only one reference [1] to it in the literature. While this condition probably is common in occurrence in the experience of all pediatrists, I am inclined to believe that it is more common in this locality and in more recent years than in some other localities and in my own earlier years, and that the manifestations are more severe.

My first impression was that this lesion was caused by rubbing against the clothing of the naturally most accessible and most vulnerable portion of the exposed glans, the meatus. This, however, seemed improbable, for it would hardly explain the deep ulceration often seen, and it was soon evident that similar lesions about the diaper region were not infrequently present at the same time. For a time attention was directed to the narrowness of the meatus as a possible cause, though we soon learned that in doing so we were looking for a cause in what was in reality an effect. Routine examination of the urine gave us no help. Only in the last year or two has the real explanation become increasingly evident. In the twenty-five or more cases seen during the past winter and spring there has been no exception to the observation that this lesion is associated with what is known as the ammoniacal diaper. I had not been aware that anyone had ever reached a similar conclusion, but on looking over Zahorsky's paper [1] on the ammoniacal diaper again I found that he had devoted a paragraph to an excellent description of the lesion in ques-

1. Zahorsky, J.: The Ammoniacal Diaper in Infants and Young Children, Am. J. Dis. Child. **10**:475 (Dec.) 1915.

tion and had also traced its origin to the ammoniacal diaper. So far as I know this is the only reference to this association in the literature.

While the condition itself is rarely, if ever, of serious import, it is nevertheless usually very troublesome and the apparent general lack of knowledge of its pathogenesis would seem to warrant its presentation. Its peculiar location, moreover, always causes deep concern in the household.

More commonly the lesion manifests itself as a rather superficial ulceration about the meatus. From what we know about the development of similar ulcers in the diaper region due to the same cause it is probably preceded, as pointed out by Zahorsky,[1] by a vesicle, though this is rarely seen before it is broken. At times the ulcer becomes deep and extensive, up to 2 mm. in depth and more than 5 mm. in width. Usually it is more or less covered by a crust which is very firmly attached over a considerable area. Surrounding the ulcer there is often an area of inflammation which involves both the adjacent surface of the glans and extends into the urethral opening with consequent narrowing. In the severer cases there are commonly present at the same time erythema, vesication and ulceration of the glans, scrotum and the rest of the diaper region wherever the diaper is in intimate contact with the skin.

SYMPTOMS

The symptomatology is evident from the pathology. The salty urine coming in contact with the denuded meatus causes acute pain when the child begins to urinate. He immediately stops urinating and cries with pain. A subsequent attempt to urinate, as the discomfort from a distended bladder forces him to try it again, leads to the same result. No amount of coaxing will induce him to try it again until the distended bladder becomes intolerable or begins to overflow. Then, having once started, the grateful relief that comes from emptying the bladder and the lessening of the pain of the first contact with the urine, will cause him to continue to urinate until the bladder is more or less emptied. Unless the condition is quickly remedied the same cycle repeats itself at the next urination. Often the emptying of the bladder is deferred for from twelve to eighteen hours. As a rule, the condition is less severe than that just described, and the child will urinate before there is very painful distention.

In some cases there is a greater or lesser degree of mechanical obstruction. The urethral opening is nearly always narrowed, often so much so that the urinary stream is threadlike and the urine can be expelled only with evident effort. I have never seen this alone cause serious obstruction. A more frequent cause of nearly complete obstruction is the scab that forms on the ulcerated area. This is very adherent and can hardly be removed without tearing and bleeding of the denuded and adjacent portion of the glans. This is practically always accompanied by a narrowing of the meatus, and it is at times impossible to tell whether the occlusion is due chiefly to the scab or to the narrowing of the urethra itself. Two cases that recently came under observation illustrate these points.

REPORT OF CASES

CASE 1.—A child, aged 2 years, was unable to empty the bladder both because of pain and obstruction and because of overdistention of the bladder. From time to time, there was a dribbling overflow that found considerable difficulty in making its exit. In spite of desperate efforts, aided by coaxing from his mother, he was able only intermittently to force out to a height of two feet two tiny divergent streams no thicker than a fine thread.

Examination showed the meatus completely covered with a firm, dry, parchment-like crust that almost completely occluded the opening, and so firmly adherent that it did not seem expedient to remove it at the time. The bladder was distended almost to the umbilicus. By continuous, gentle pressure over the bladder, and with much coaxing to voluntary effort, we were finally able to empty it almost completely through the two minute openings. If pressure over the bladder was stopped for a moment, the flow would stop immediately as if the bladder had been paralyzed by the overdistention.

CASE 2.—A boy, aged 2½ years, was apparently unable to empty the bladder, probably both because of pain and of great narrowing of the meatus. The opening was barely visible, being so small that it would hardly have admitted a fine needle. The meatus itself was apparently narrowed to this degree and was further covered by a tough skinlike crust that had to be removed, but only at the expense of considerable pain and some blood and adjacent epidermis. Even then the meatus could barely be made out, and it was difficult to see how the bladder could be emptied through it.

A permanent narrowing of the meatus, analogous to a stricture, apparently never occurs even after repeated and prolonged ulceration. In the two cases just cited, after appropriate treatment, the urinary stream was apparently of normal caliber on the following day. The restoration to a normal condition is commonly as rapid as the original production of the lesion itself.

One other symptom occasionally causes great concern to the mother but is never serious. If the ulceration is deep and extensive, there is, at times, a little hemorrhage especially noticed at the end of urination. It is surprising that this does not happen oftener when one considers the great vascularity of the glans.

The ammoniacal diaper that apparently always causes this condition of the meatus is to me still surrounded with mystery in spite of its common occurrence. Clinically it manifests itself as follows. An infant or young child that has, perhaps, attracted no attention to its general health or its state of nutrition, or digestion, except that it is constipated, is noticed when changed at night or in the morning, to have a very strong odor of ammonia about the wet diaper. This odor is not simply one detectable on close effort. The fumes are comparable to those that escape from a bottle of ammonia. They are distinctly irritating to the nostrils, and even cause a biting sensation in the eyes as one stoops over the open diaper. This condition is rarely noticed, except at night and most often toward morning. If the urine of such a child voided later is allowed to stand in a vessel no odor of ammonia is detectable even if it is kept at body temperature. Sometimes, the condition is present every night, continuously and consecutively, as in a case I saw recently, for over a year. Again, it is apparently absent, or barely noticeable, for weeks and months, only to appear again without any known change in health or in food, with violent manifestations. In one of my own children during the second year the condition would occasionally appear in mild form, then be absent for weeks or months. Suddenly at night, without premonition, or any known provocation, the child would wake up toward morning screaming with pain, the diaper would be almost intolerably strong of ammonia, and the whole diaper region would be reddened and painful as if scalded, and covered with blisters. In a day or so without any treatment the condition would disappear as mysteriously as it came, only to reappear at a subsequent time, perhaps for a longer stay. The condition is apparently much more frequent in private homes than in hospital wards.

Many children have this ammoniacal diaper for weeks and months without any other unpleasant symptoms. Usually it produces at least a local redness and subsequent desquamation of a large part of the diaper region. In severer cases there is scattered vesication and ulceration. These ulcers often remain denuded for a long time, often

they heal over but remain as discrete nodules during the whole time that the ammoniacal condition persists. Often the exposed meatus is the only seat of a deeper lesion; rarely it escapes; as a rule, it is involved with the rest of the diaper region.

For the production of skin lesions contact with the wet ammoniacal diaper is apparently always necessary. The word diaper is, of course, here used in a generic sense and includes any article of clothing, or bedding. The skin is always most irritated where the contact is most intimate and prolonged—over the buttocks and lower back, from lying, and across the abdomen and about the thighs above the knees, because of the tighter application of the diaper. The male meatus is peculiarly exposed to such contact, and the delicate mucous membrane is the most vulnerable spot; the female meatus is well protected and is apparently rarely if ever involved. The effect of contact was well illustrated in the first case cited above. For several nights the child did not wet the diaper and the ulcer healed. A few days later he was again unable to urinate because of a new ulceration of the meatus. Without any questioning the mother said that he had wet his underclothing over a small spot with urine and that contact with this spot had apparently brought the trouble on again. The favorable effect that follows dispensing with the diaper at night further confirms this view.

AGE INCIDENCE

The age incidence of this condition is of special interest. It is almost unknown in the nursing baby, though I have seen it in a baby on mixed feeding; is relatively rare in the first six months, and is only exceptionally encountered before the third or fourth month. It is much more common in the latter half of the first year; probably attains its maximum frequency and severity during the second year; becomes less common during the third year, and vanishes soon after this. The lesser incidence after the third year is probably due to the greater infrequency of bed wetting without which it would not be recognizable.

TREATMENT

The treatment of this condition naturally is directed to the lesion itself if it is present, and to the prophylaxis and treatment of the ammoniacal diaper.

If the meatus is ulcerated or crusted over to some extent, and there is no obstruction, the proper therapy would seem to consist in applying thickly some substance like petrolatum that would coat over the involved area so that urination may be less painful and so that there will be protection on contact with the diaper. When the meatus is acutely inflamed, the opening narrowed and covered with an obstructing scab, and urination is difficult and peculiarly painful because of the inflammatory condition, a wet boric acid dressing has always quickly relieved the urgent indications. Gauze wet with the solution is fluffed over and about the penis, this is covered with a thick layer of cotton extending beyond the gauze to keep it in place, and over this the diaper is pinned snugly. The gauze is kept wet with the solution and is changed after each urination. The relief from this procedure has been unfailing and almost instantaneous. Dispensing with the diaper at night often has a favorable effect in preventing new lesions and in allowing old ones to heal. Mechanical dilatation has never been necessary. Neither has catheterization, which would be strongly contraindicated unless absolutely unavoidable.

If the scab itself is causing obstruction, or if it can be removed without injury to the adjacent tissues, this should be done. This is facilitated by the previous application of petrolatum or a wet dressing.

The cautious application of a very weak solution of cocain to the ulcerated area in case the child will not urinate because of pain would seem rational and unobjectionable, though the remembrance of a former attempt to urinate might lessen its usefulness.

The prophylaxis of the ammoniacal diaper presupposes a knowledge of its pathogenesis. To my mind we do not possess this knowledge at the present time with complete clarity.

The more inviting theory is that based on the work of Keller and others that in certain nutritional disturbances due to the ingestion of cow's milk fat beyond the infant's tolerance there is produced a relative acidosis of enteric origin which manifests itself in the urine in the excretion of a hypernormal amount of ammonium salts. This view has been formally championed by Southworth,[2] who reported a number of cases presenting this clinical picture and the patients were relieved of this symptom when the fat was reduced to an adequate degree. He also reported a similar result from the administra-

2. Southworth, T. S.: The Ammoniacal Diaper and Its Correction, Arch. Pediat. **30**:10 (Oct.) 1913.

tion of alkalies, favoring potassium, calcium and magnesium bases over those of sodium. The cases detailed by Southworth were nearly all in younger infants in whom there was a definite clinical picture of overfeeding with fat or with milk and the therapeutic results would seem to leave little doubt as to the nature of the primary condition that produced the ammoniacal diaper in these cases.

I am inclined to believe that this explanation may be accepted as one factor in the case of younger infants fed exclusively on the bottle. This might further explain the greater frequency of this condition in my own cases for it has been my practice in recent years to give relatively more milk and less carbohydrate in the bottle feedings than formerly. In fact, the condition has been so frequent in my own cases that I have even assumed it to be within the range of normal and have used no measures to relieve it unless there was definite skin irritation. Even in these cases, however, where a dietetic relationship seems most evident I have been struck by the frequency with which neither reduction of the fat by lessening the milk or by taking off the cream nor the use of alkalies leads to an appreciable therapeutic result.

It seems to me, however, quite impossible on this hypothesis alone to explain the occurrence of the ammoniacal diaper in a very large number of cases. It is, for example, a well known fact that the ammoniacal diaper occurs with greater regularity when dried milk is used than with almost any other food. In my own experience, the severer manifestations, such as vesication and ulceration, occur more frequently in older children who are on a liberal diet and are getting very little milk. One of the most severe and protracted cases I have seen with extensive ulceration of the meatus, scrotum, and, in fact, of the whole diaper region, was in a child, aged 2½ years, that was on a general diet and getting only a pint of skimmed milk. In some cases the mothers have stated that these older children were getting practically no milk at all. Cutting down the milk or removing the cream, even to a marked degree, has in the case of older children been quite disappointing from a therapeutic standpoint. The use of alkalies has given the same impression.

DISCUSSION

It is interesting in this connection to note that the ammoniacal diaper occurs less frequently and less severely with cream mixtures

than with simple whole milk mixtures, or even, as has been pointed out, with dried skimmed milk mixtures. If this observation is correct, then the fat alone cannot account for the condition. This is further borne out by the relative freedom from this symptom when albumin milk is given in spite of its high fat content. It will be recalled that Czerny and Keller's "milchnährschaden," which is apparently due to an excess of fat in the infant's food and in which there is a heightened urinary excretion of ammonium salt, is produced when whole milk is fed in excess of tolerance. Certainly, it does not occur as definitely with cream mixtures, in spite of the fact that fat is assumed to be the factor that causes it. It will be recalled further that Czerny and Keller state that the soap stool does not occur with cream mixtures and they offer the ingenuous explanation that this is due to the fact that it is difficult to get cream that is not "zersetzt," that is, unfavorably influenced by bacteria.

To me it seems more reasonable that while the symptom under discussion may be due to the fat, at least in that class of cases where there is clinical evidence of overfeeding with fat, that fat will cause it only in certain combinations, and only if certain other food-elements are represented in certain relative ratios to the fat. Thus, in a milk mixture it occurs less frequently if the fat is relatively higher than the protein and the salts as compared with their normal relative representation in whole milk; and more frequently if the normal proportion is maintained, or even if the fat is relatively lower than the protein and the salts. The fact is not sufficiently emphasized that the different food elements cannot be considered as isolated factors but must always be considered in relation to the other food elements in the causation of clinical pictures.

While the fat within these limitations may account for an increased excretion of ammonium salts in a certain proportion of these cases, and may thus supply one factor in the pathogenesis of the ammoniacal diaper, I do not believe that it accounts for all or most of them. Even in those cases where the fat would seem most clearly the causal agent, it is impossible to exclude the protein, or even the salts as a factor. I have gained the impression that, in the production both of the clinical picture of "milchnährschaden," and of the ammoniacal diaper, it is not so much a matter of amount of fat as of the amount of milk even if it is partly skimmed. The protein and the salts, if this observation is correct, would command attention and especially, of

course, the protein. This would explain many phenomena that cannot be accounted for on the assumption that the fat is the main factor. It would explain the frequency of the ammoniacal diaper when Dryco Milk is used in spite of its low fat content because as commonly used the amount of protein is relatively considerably higher than with ordinary fresh milk mixtures. Assuming that a milk from which two thirds of the fat has been removed is reduced to about one eighth or one ninth its volume in the process of desiccation, and that eight level tablespoonfuls of the dried product represent one ounce by weight, then one level tablespoonful would equal approximately one ounce of fresh milk, skimmed to a nearly equal extent. In giving two and one-half or even three tablespoonfuls of the dried milk to each pound of baby, as is commonly done, one would give the protein and salt equivalent of at least from 2½ to 3 ounces of milk to the pound of baby which would represent a much larger amount than is ever used in feeding fresh milk. This might also explain the greater frequency of the occurrence of the ammoniacal diaper in my own experience in more recent years during which I have been feeding more milk, that is, more protein and less carbohydrate. On this basis, too, one might find a satisfactory explanation for those cases in older children that are on a nearly general, almost fat free, diet.

The failure of ammonuria to occur, except in connection with the wet diaper in situ, together with the peculiar behavior of the ammoniacal diaper would suggest a further nondietetic factor residing in the diaper itself. A hyperexcretion of ammonium salts cannot alone be assumed to account for the ammoniacal diaper. We have here not combined but free ammonia. The ammonium salts that would be present in this condition are fairly stable, and it is very doubtful whether the evaporation of the urine would be carried to a point where ammonia would be liberated to the extent found in these diapers. It is well known that certain alkalies break up ammonium salts and liberate free ammonia. On this basis Zahorsky,[1] after failure to combat the condition by lessening the fat in the food and by the use of alkalies therapeutically, came to the conclusion that "the immediate cause of the ammoniacal diaper is the presence of an alkali in the diaper, or the bedding." This alkali he traced to "strong alkaline soap that had not been rinsed thoroughly from the diapers, or bedding, or to the presence of an alkaline stool, or to the possible presence of lime in the dried diaper in locations like St. Louis where the lime content of the water is high."

Zahorsky's explanation was distinctly appealing in that it alone, apparently, could account for the mysterious vagaries of the ammoniacal diaper; the startling appearance and sudden disappearance without known change in food or in health; the invariable association with the wet diaper in situ only; the failure of dietetic and alkaline treatment in many cases; and the greater incidence and severity of the symptom in older children which he also noted. Unfortunately he contented himself with saying: "It is not necessary to give the details" and presented no evidence. That soap, lime, and an alkaline stool do not explain the condition in a great many cases can easily be demonstrated by excluding these factors experimentally.

Other agents, however, may produce the same result and the action of bacteria naturally suggests itself. Thus in a recent personal communication Zahorsky says: "The diaper or the bedding, infected by an enormous number of bacteria, not boiled daily, must also be considered." The thought would suggest itself further that bacteria might liberate ammonia, not directly or indirectly from the ammonium salts in the urine, but from the urea. It is well known, for example, that *Micrococcus ureae,* and probably also other organisms in the urine, act on urea with the liberation of ammonia. As suggested by Kendall in a personal communication, the large evaporating surface presented by the diaper as compared with the small surface in the test tube would naturally lead to the freeing of a comparatively larger amount of ammonia. These considerations would lead us back again to the clinical impression already recorded that the determining factor in those cases in which the dietetic factors are easily grasped is the amount of milk given even if skimmed; that is, of protein, rather than, say, the amount of fat. More milk carries with it more protein and an increased excretion of urea for bacteria to act upon.

The further question would naturally arise whether a hyperexcretion of ammonium salts, or of urea, due to an excess of either the fat or the protein in the diet, is a prerequisite to the production of the ammoniacal diaper; or whether something in the diaper itself is sufficient to elicit the condition in a normal urine. So far as I know, the answer to this question is not yet at hand. The fact that free ammonia occurs with great regularity with certain foods, and an excessive amount of fresh milk such as Dryco milk, would point to the conclusion that the diaper alone is not sufficient to bring out this symptom unless there is an abnormal urinary condition. The

occurrence in older children on a general diet makes it hard to assume an abnormal urinary factor and would suggest that the diaper can cause it even if the urine is normal. The invariable association of this symptom with the diaper would again suggest the diaper as the important factor and especially in these cases where the symptom occurs erratically. Some further observations made by Zahorsky are interesting but inconclusive in this connection. He found that "the ammonia content of the urine was relatively higher in older children than in infants," and "while rather high in children presenting this symptom (ammoniacal diaper) not higher than in many who did not present it." He found further that "all but one of the patients so examined," that is, those having ammoniacal diapers, "showed the ammonia nitrogen higher in the morning after the night's rest." The fact that the ammoniacal diaper is rare in hospital cases as compared with those in private practice can be accounted for on either basis. In hospitals all diapers are thoroughly sterilized for obvious reasons, while in homes this is commonly omitted. On the other hand, it is also true that hospital babies, as a rule, can stand less milk than babies in private practice and so the dietetic factor is reduced to a minimum.

While our knowledge of the whole subject lacks precision and finality, nevertheless it gives us a definite line of treatment. The prophylaxis of the ammoniacal diaper and so of the ulcerated meatus, in accordance with our present state of knowledge, would consist then, in the avoidance of an excess of milk in the diet and a compensating use of the more tolerable carbohydrates, the dextrin-maltose preparations in younger infants, and these together with the starches in older infants. The treatment would consist in the reduction of the amount of milk; the increase, if permissible, of the carbohydrates; together with the use of such alkalies as milk of magnesia, lime water, or potassium salts. In selected cases malt soup best meets all of these indications. In older children on a general, nearly milk free diet, the dietetic treatment is still baffling in my own experience. The indications on the part of the diaper would be met by thorough rinsing and thorough boiling daily of all diapers and night clothes, possibly even the bedding.

The bearing of this lesion on the question of circumcision is perhaps evident.

CONCLUSIONS

1. An ulcerated meatus in the circumcised child only is a frequent symptom.

2. The "ammoniacal diaper" is the cause of this lesion.

3. The etiology of the "ammoniacal diaper" is still obscure but seems due to one or both of two factors: a dietic error that increases the ammonium or urea content of the urine, and the presence of an alkali or of certain bacteria in the diaper.

4. The treatment consists in correcting, if possible, the dietetic error and in thorough rinsing and boiling of the diapers, night clothes and bedding.

DISCUSSION

DR. KERLEY: Dr. Brennemann has described a condition that is fairly frequent in office practice. I always classify these cases as eczema of the meatus. I never feel that they are of very much significance as they get well very easily. As far as the ammoniacal diaper is concerned, a great many of these cases cannot be accounted for on this ground. My treatment consists in giving citrate of potash, 60 to 80 grains a day, and applying an ointment of 5 per cent. boric acid. That is all I have had occasion to do, and it is rare not to have the child come back within a week practically well. I have not found it necessary to pay much attention to the diet. I have had no case in which there was a permanent constriction of the urethra, and no case to occasion more than some disturbance in urination. All cases I have seen occurred in children who had been circumcised, and it is not at all infrequent to find it a short time after circumcision, from three to six weeks following the operation.

DR. HEIMAN: Several years ago Goldenberg described a condition which he called dermatitis erythema meatorum and he asked me whether I had had any experience with this condition. I told him it was a very common occurrence and that I did not attribute it to acidity of the urine any more than I attributed enuresis to that cause. I told him it was simply a traumatic condition and he published it as such in his article. As to the treatment, I have never paid any attention to the ammoniacal condition of the diaper, but have treated it by applying pure nitrate of silver. In some there is a circular ring somewhat like herpes around the meatus and I think we may assume that there is a secondary infection. I advise the mothers to use another piece of linen inside the diaper. Priapism occurs quite frequently and that causes irritation. The silver nitrate is the first thing I use and then 10 per cent. balsam in castor oil.

DR. SCHLOSS: I agree with Dr. Brennemann that this condition is frequently annoying and difficult to cure. As to its exact pathogenesis I have nothing to add. In my experience in examining the urine there has been a high ammonia coefficient and hyperacidity. I think that where the food contains a high percentage of protein, as in dried milks, the condition may be helped by giving larger amounts of alkali and relatively high amounts of carbohydrate.

DR. MARRIOTT: A word regarding the ammoniacal diaper. The ammonia which is present does not occur in the urine when passed, as the kidney does

not secrete a urine containing any free amount of ammonia. The ammonia is produced after the passage of the urine and must be the result of the breaking down of either ammonium salts or urea. Ammonium salts are increased in certain types of feeding and these salts may be broken up by the action of alkali, either of soap left in the diaper or as the result of standing with alkaline soap stools. The more important factor in the production of ammonia in the diaper is bacterial decomposition of the urine, either of the urea or the ammonium salts. Quite a number of bacteria are capable of doing this and when the diaper and the child's buttocks become infected with these organisms ammonia is produced very shortly after the passage of the urine. This can be prevented if the diapers are thoroughly boiled. It is also advisable to attempt to clean off the child's buttocks and perineal region thoroughly. When this is done the ammonia production will often cease without resorting to any change of diet.

DR. GRIFFITH: These cases, as well as any other irritation of the external genitals, may often be, at least temporarily, relieved by removing the irritation caused by the diaper. The ordinary triangular-shaped diaper is frequently far too thick and far too tightly applied. In instances of irritation I have at times made use of the diaper which is used by a considerable number of the foreign element of the population; one which is square, and in which the two lower corners are brought up, one on each inner side of the right and left thigh respectively, and pinned to the diaper above the hips. This removes entirely the element of pressure and irritation.

DR. BRENNEMANN: In reply to Dr. Kerley, who says he considers this condition a trifling affair due to an eczema and not at all bothersome, and to Dr. Heiman who thinks it due to traumatism and of not much importance, I can only say that those statements confirm the view that I have expressed in my paper that this condition is more frequent and more severe in this locality than in other places and in our own past experience. With us the ammoniacal diaper is very common and the ulcerated meatus which results from it has given us a lot of trouble. Many of our cases are not of that mild sort that get well quickly; in many of them it has taken us a long time to get rid of them. As to the discrepancy in my remarks pointed out by Dr. Kerley, that this condition is a diaper phenomenon and yet that it occurs very frequently after the second year when diapers are no longer worn, I would say that I used the word diaper in a sort of generic sense to include bedding, pads, nightclothes, etc., as I stated in a part of my paper that was omitted. I can only say that I, too, passed through a stage when I believed the condition was due to eczema, trauma, or narrowing of the meatus. As to whether the ammoniacal diaper caused the lesion I would suggest to Dr. Kerley and to Dr. Heiman that if they made it a practice, as I have done in recent months, to ask the mothers whose children present this lesion whether the diaper smelled of ammonia at night they would very regularly get the answer "I should say so—it is something terrible!"

As to the remarks of Dr. Marriott concerning the ammonium salts and the liberation of ammonia, that was mentioned in a part of my paper that was omitted, it certainly seems probable that there is some factor in the diaper itself that causes the ammonia to be liberated. That it is not commonly an alkaline stool, or an alkaline soap or lime, can easily be demonstrated. The bacterial factor would seem the only one left on that hypothesis, though it seems to me that the evidence is not yet conclusive. There are still some details that must be worked out.

BLOOD VOLUME IN INFANTS ESTIMATED BY THE VITAL DYE METHOD*

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This report is part of a study which is now being carried on in the pediatric department on the problem of the anemias of infancy and childhood. Many studies have been made in this field but most of the work so far done has reference mainly to the blood picture, studies relating to the differential count of the white blood cells, the study of the red blood cells, their number and fragility and to the percentage of hemoglobin; in many instances the postmortem findings are added to these studies of the cells and hemoglobin. All these studies are valuable and have their place in the problem of the anemias but so far they have led to little more than an unsatisfactory classification of the anemias. Even as regards classification there is much confusion and very little has been ascertained as to the etiology of the various anemias which occur so frequently during infancy and childhood. Today we can do little more than divide anemias into primary and secondary groups. We know little as to the specific causes of these anemias. We know the end results well but what has brought about these results we know little of and it would seem that we are likely not to go much further in our understanding of these blood conditions unless we attack the problem from a somewhat different standpoint.

During the past few years a great deal of experimental work has been done on blood, regarding it as an organ. Blood regeneration following certain measures used to injure or modify the functioning of the bone marrow and spleen, as certain bacterial toxins, certain chemical poisons as benzol and saponin or the administration of over exposure to roentgen-ray and radium, have been studied carefully.[1]

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*From the Departmnet of Pediatrics, University of California Medical School.

1. Whipple, et al: Series of articles on Blood Regeneration Following Simple Anemias, Am. J. Physiol., 1920.

These investigations have thrown a good deal of additional light on many of the functions of the blood and blood forming organs. The rate of regeneration of the red blood cells is fairly definitely known. The capacity to regenerate following certain of these procedures has also been carefully investigated and we have data now of considerable importance on these points.

The many studies on coagulation have differentiated the various factors which enter into this complex function. From the results of these studies we are now able to group various types of hemorrhagic conditions, according to which factor, salt, prothrombin, platelets, fibrinogen, antithrombin, is disturbed. By these means our understanding of these puzzling conditions has been greatly clarified and our measures for combating or favorably effecting them has been materially advanced.[2] The close relationship of some of these hemorrhagic conditions, such as purpura hemorrhagica, to the group of the little understood primary anemias, aplastic anemias, has been pointed out by Minot.[3]

Equally important are the studies on pigment production and destruction in the blood for a better understanding of the functions of blood considered as an organ. The part the liver plays on this pigment formation has been carefully worked out by Whipple and his associates [4] in their anemia studies on bile and plood pigment. They have pointed out the part the liver plays in pigment formation. So far, clinically, little or no attention has been paid to hemoglobin beyond the estimation of the percentage of hemoglobin found in various blood disturbances. Unfortunately, most of the numerous reports are based on inaccurate methods of estimating hemoglobin and this notwithstanding the fact that Van Slyke,[5] and Palmer [6] and more recently Robscheit [7] have pointed out the inaccuracies of older methods and the latter has described a simple accurate adaptation of their methods for clinical use.[7] They have shown that the estimation of hemoglobin by the Tallqvist methods and others now in common clinical use

2. Hurwitz, S. H., and Lucas, W. P.: A Study of the Blood in Hemophilia, Arch. Int. Med. **17**:543 (April) 1916.
3. Minot, G. R.: Arch. Int. Med. **19**:1062 (June) 1917.
4. Whipple et al: Series of articles on Blood Regeneration in Am. J. Physiol., 1920.
5. Van Slyke, D.: J. Biol. Chem. **33**:127, 1918.
6. Palmer: J. Biol. Chem. **41**:209, 1920.
7. Robscheit, F. S.: J. Biol. Chem. **41**:209, 1920.

TABLE 1.—Chart A. Of Thirty New-Born Infants' Blood Volume Estimations from Two and One-Half Hours to Fifteen Days. In Most Cases Only Single Computations for Each Case Were Made

No.	Age	Sex*	Birth Weight	Weight Day of Blood Volume	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume C.c.	Blood Volume, C.c.	Blood per Kg. C.c.	Pigment Volume	Hb., per Cent.	Red Blood Cells	Weight Day Following Blood Volume	Disc. Weight 14th Day	Reaction	Length at Birth, Cm.	Remarks
6830	30 hrs.	♂	3,560	3,495	11.3	28.0	70.5	152	542	155	672	124	6,480,000	3,330	3,680	None	52	
6639	12 hrs.	♂	3,915	3.860	11.3	48.5	49.5	214	441	114	432	98	5,640.000	3,700	3,615	None	53	
6771	28 hrs.	♀	2,900	2,830	12.5	38.4	61.5	169	441	157	467	106	7,200,000	2,790	3,250	T 37.4	50	
6771	15 days	♀	2,900	3,270	11.3	53.0	46.0	247	465	142	348	75	.....	3,250	3,250	None T 38.5	50	
6619	11 days	♀	2,650	2,550	11.2	50.0	49.1	170	340	133	306	90	4,290,000	2,550	2,610	Drowsy	49	3 minutes late, obtained dyed blood
6786	5 hrs.	♀	3.370	3,370	11.4	34.2	63.0	184	540	160	615	114	4,730,000	3,430	3,765	None	51	
6723	8 hrs.	♀	2.710	2,710	8.1	41.3	56.5	193	469	173	483	103	.....	2.510	2.675	None	50	
6820	48 hrs.	♀	3,745	3,560	12.2	44.7	54.0	264	590	165	601	102	5,080,000	3,580	3,625	Vomited dur. B. V.	52	
6785	32 hrs.	♂	3,710	3,620	11.3	42.0	57.0	263	627	173	664	106	5,050,000	3.625	4,080	None	53	
6816	24 hrs.	♀	3,390	3,470	12.2	37.3	61.4	252	676	195	770	114	.....	3,535	3,790	T 37.8	52	
6628	9 days	♂	3.080	2,890	10.7	41.5	57.5	154	372	129	405	109	4,660,000	2.845	2,935	None	49	
1482	3 days	♂	3,220	3,150	9.8	42.9	56.0	156	364	116	382	105	5,644,000	3,170	3.410	None	50	
6904	3 days	♀	3,150	3,060	10.75	46.5	52.0	177	382	125	...	...	.....	2,950	3,325	None	50	
6090	4 days	♂	3.420	3,410	12.0	46.3	52.5	204	440	125	...	...	.....	3,320	3,550	None	53	
6712	10 hrs.	♀	3.010	2,890	12.4	45.5	53.6	160	354	122	354	100	5,060,000	.....	.....	.....	50	Died jaundiced
6622	4 days	♂	3.850	3,740	10.5	36.7	62.3	199	545	146	588	108	5,992,000	3,700	3,765	None	52	
6310	5 days	♀	2.980	2,980	12.0	42.5	56.75	192	454	152	444	98	.....	2,960	3,190	None	51	
6670	6 days	♂	3,400	3,300	11.8	42.8	56.0	209	490	149	534	109	5,420,000	3.240	3.515	None	50	
6812	15 hrs.	♂	3,275	3,275	11.75	37.8	59.5	136	361	110	393	109	5,140,000	3,200	3,310	None	51	2 minutes late, obtained dyed blood
6801	2½ hrs.	♀	3,350	3,350	8.6	36.0	61.6	184	513	155	523	102	.....	3,120	3,080	None	50	
6948	14 hrs.	♀	4,465	4,460	12.25	33.0	65.3	283	857	192	899	105	.....	4,390	4,280	None	53	2 minutes late
Schn.	36 hrs.	♀	3,320	3,160	10.3	40.0	58.0	204	507	161	496	98	.....	3,200	.....	None	52	
Flax.	32 hrs.	♀	3,030	2,950	10.6	41.5	57.0	137	331	112	307	93	4,648,000	3.010	.....	T 37.4	49	
Turt.	26 hrs.	♀	3,325	3,230	8.8	37.5	61.5	142	378	117	359	95	.....	3,290	.....	None	49	
Kan.	3 hrs.	♀	2.980	2.980	11.5	35.7	53.4	159	446	150	...	...	.....	2,850	.....	None	51	
2743	6 hrs.	♂	4.130	4,130	11.75	31.0	67.0	202	595	144	702	118	5.696,000	.....	.....	None	56	
Tiff.	12 hrs.	♀	3,845	3,720	11.2	43.7	55.3	245	566	153	549	97	5,552,000	3,720	.....	Cyanotic drg. test	54	2 minutes late, obtained dyed blood
Carl.	49 hrs.	♂	2.800	2,950	10.5	35.7	62.8	227	635	188	857	135	5,520,000	2,950	....	None	49	
Kado.	24 hrs.	♂	2,880	2.880	10.25	30.7	67.2	170	553	192	635	115	5,464,000	2,975	.....	None	50	
Kayr.	17 hrs.	♂	3,550	3,390	10.8	51.9	46.3	188	363	107	304	84	.....	3,310	.....	None	51	3 minutes late

* In this column, ♂ signifies male, and ♀ female.

have an inaccuracy of from 15 to 30 per cent. which in some cases runs as high as 50 per cent. from a correct estimation of hemoglobin as done by the Palmer modification.

Before one can even begin to make a study of the anemias there are certain questions that must be definitely answered, questions for which we have at present no normal standards. It is first necessary to obtain figures on which to base our studies. We have been fortunately placed for making these studies on anemias of infancy and childhood because for the past three years researches on these problems have been in progress and are now in progress at the Hooper Foundation for Medical Research.

One of the first of these questions to be settled is that of a normal blood volume in infancy and childhood. It is needless to point out that we cannot go very far in any comprehensive understanding of the blood as an organ without some idea as to the volume of blood normally in circulation, its normal variations at different periods and under varying conditions of nutrition and growth. The first point we have attempted to arrive at any conclusion on is the normal blood volume in infancy. This paper deals mainly with the normal variations during the first year. We have only a few examples of blood volumes in infants suffering from some form of secondary anemia.

HISTORICAL

Keith, Rowntree and Geraghty[8] first used the dye method for estimating the blood volume. In their studies they used vital red and demonstrated that the normal blood volume for adults is about 8.8 per cent. or 1-11.4 of the body weight. Unfortunately, their supply of dye was limited and on account of the war they were unable to procure more to carry on their studies.

For several years Dr. Herbert M. Evans has been studying the various dyes in his investigations on vital tissue staining. From his work he was able to suggest that brilliant vital red would most probably be the dye best suited for blood volume studies. Dr. Whipple and his associates have tested this dye out in many hundreds of experiments and have found that it answers the requirements for a satisfactory dye. First, because it is nontoxic when injected intravenously, even in large doses fifteen times that used in the estimation

8. Keith, Rowntree and Geraghty: Arch. Int. Med. **16**:547 (Sept.) 1915.

of plasma volume. Second, this dye is not taken up by any of the red blood cells or tissues but remains for a comparatively long time in the plasma but the ultimate fate of the dye is not known. Third, it can easily and accurately be determined by colorimetric methods. The use of this dye in dogs has shown that the normal healthy growing dog has an average blood volume of 10.1 per cent. body weight. So far as we know this method has not been applied to infants or children. During early infancy this method can be easily carried out by using the longitudinal sinus, and thanks to the Goldbloom [9] block we have a safe device for the accurate injection of dye. Without this block the work would have been much more difficult, in fact we started some of these studies before we were able to secure this simple device and we can testify that it has facilitated our work and made us feel far more confident in persisting with the repeated injections of the dye on so many cases. In working with new-born infants this block is indispensable. The sinus was used by us in all our studies, except the few we have done in children over 18 months old. In these older children we have used either the jugular veins or the veins at the elbow, the latter where they are large enough, we have found easier to work with than the jugular veins, for as will be seen there is a certain minimum of manipulation necessary in changing syringes which makes it difficult to use the neck veins.

PROCEDURE

Ten c.c. of blood are withdrawn into a Record syringe which has been sterilized and thoroughly washed out with sterile salt solution. This first sample of blood is immediately discharged into an accurately calibrated 15 c.c. centrifuge tube (hematocrit tube) which contains 2 c.c. of a 1.6 per cent. solution of sodium oxalate;[7] the blood and oxalate are thoroughly mixed by inverting the tube several times so as to obviate any possible clotting. The centrifuge tube is then stoppered. From this tube the hematocrit readings are made and the serum for making the standard control dye mixture is taken. Before this first sample of blood is taken the standard amount of dye solution is drawn up into a Record syringe along with enough physiologic sodium chlorid (0.9) solution to make sure that all the dye has been taken up into the syringe from the small containing dish in which the measured amount of dye is placed.

9. Goldbloom, A.: Am. J. Dis. Child. **16**:388 (Sept.) 1918.

The dye solution is a 1.5 per cent. solution and is given in the amount of 1 c.c. per 5 kg. of body weight, which gives 3 mg. of the dye per kilogram. The dye solution is injected into the sinus, immediately after the first 10 c.c. of blood have been withdrawn, using the same needle, only changing the syringe, the dye being completely washed out by drawing blood back and forth several times into the syringe after the dye has been emptied out of the syringe into the sinus. We have found this the most convenient and satisfactory way of being sure that all the dye had been delivered into the sinus. We have had no untoward happenings while following this method. The needle is then withdrawn; exactly four minutes after the injection of this dye a clean needle is again inserted into the sinus and a sample of 16 c.c. of blood is withdrawn and discharged immediately into two petrolatum lined test tubes about equally distributed. This furnishes the plasma for the estimation of the blood plasma volume. All the tubes are now placed in the ice chest for at least half an hour, then centrifuged at 2,500 revolutions a minute for half an hour. In the hematocrit tube, (accurately calibrated centrifuge tube) the total amount of fluid is noted and the number of cubic centimeters of blood cells, red and white, are noted. This gives the total hematocrit reading when 2 c.c. is subtracted for the oxalate dilution and the hematocrit reading for the red blood cells. Five c.c. of this serum are pipetted off and to this is added 5 c.c. of a 0.9 per cent. sodium chlorid solution and 5 c.c. aqueous dye solution. This dye solution is made up as follows: 0.5 c.c. of a 1.5 per cent. brilliant vital red is pipetted into a 100 c.c. volumetric flask which is then filled up to the mark with distilled water. This gives the standard against which is read the unknown dye colored plasma. The dye colored serum is pipetted off from the petrolatumed tube and 2 c.c. of this serum is diluted with 4 c.c. of a 0.9 per cent. sodium chlorid solution, which gives the same dilution to this serum as the standard dye solution made from patient's dye free plasma, to which has been added a known amount of dye and salt solution.

After mixing thoroughly, the standard dye-plasma solution and serum solution are allowed to stand for fifteen minutes, so that the intensity of color may be uniform. The standard dye solution is then put into the colorimetric wedge (we have used in all our work the Hellige colorimeter and have found it perfectly satisfactory. It has been tested against the Duboscq and found accurate) and each

of the samples of the unknown serum dye solution is read against this. The average of three readings is taken as the color percentage of the sample.

COMPUTATION RESULTS

From the hematocrit readings the plasma per cent. and the red cell per cent. may easily be calculated—the red cell hematocrit reading is read from the hematocrit tube, taking the total hematocrit reading minus 2 and the plasma hematocrit reading by subtracting the total cell hematocrit reading from the total hematocrit reading minus 2.

$$\text{Plasma volume in c.c.} = \frac{\text{Weight in kilograms} \times 40}{\text{Average colorimetric reading}} \times 100$$

$$\text{Blood volume in c.c.} = \frac{\text{Plasma volume}}{\text{Plasma per cent.}} \times 100$$

The plasma per cent. means the per cent. of the whole blood which the plasma constitutes and is obtained by dividing the total number of cubic centimeters of oxalated plasma present in the hematocrit tube

TABLE 2.—CHART B: OF THIRTY NEWBORN INFANTS, BLOOD VOLUME ESTIMATIONS FROM TWO AND ONE-HALF HOURS TO FIFTEEN DAYS. GROUPED ACCORDING TO AGE

Age	Weight in Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Gain or Loss Before Blood Volume
3 hrs.	3,350	8.6	36.0	61.6	184	513	155	None
3 hrs.	2,980	11.5	35.7	63.4	159	446	150	None
5 hrs.	3,370	11.4	34.2	63.0	184	540	160	None
6 hrs.	4,130	11.75	31.0	67.0	202	595	144	None
8 hrs.	2,710	8.1	41.3	56.5	193	469	173	None
10 hrs.	2,890	12.4	45.5	53.6	160	354	122	None
12 hrs.	3,720	11.2	43.7	55.3	245	566	153	—120 G
12 hrs.	3,860	11.3	48.5	49.5	214	441	114	— 55 G
14 hrs.	4,460	12.25	33.0	65.3	283	857	192	None
15 hrs.	3.275	11.75	37.8	59.5	136	361	110	None
24 hrs.	3,470	12.2	37.3	61.4	252	676	195	—120 G
24 hrs.	2,880	10.25	30.7	67.2	170	553	192	—165 G
26 hrs.	3,230	8.8	37.5	61.5	142	378	117	— 95 G
28 hrs.	2,830	12.5	38.4	60.0	169	441	157	— 70 G
30 hrs.	3,495	11.2	28.0	70.5	152	542	155	— 65 G
32 hrs.	2,950	10.6	41.5	57.0	137	331	112	— 80 G
32 hrs.	3,620	11.3	42.0	57.0	263	627	173	— 90 G
36 hrs.	3,160	10.3	40.0	58.0	204	507	161	—160 G
48 hrs.	3,560	12.2	44.7	54.0	264	590	165	—185 G
49 hrs.	2,950	10.5	35.7	62.8	227	635	188	+150 G
3 days	3,060	10.75	46.5	52.0	177	382	125	— 90 G
3 days	3,150	9.8	42.9	56.0	156	364	116	— 70 G
4 days	3,740	10.5	36.7	62.3	199	545	146	—110 G
4 days	3.410	12.0	46.3	52.5	204	440	128	— 10 G
5 days	2,980	12.0	42.5	57.0	192	454	152	None
6 days	3,300	11.8	42.8	56.0	209	490	149	—100 G
9 days	2,890	10.7	41.5	57.5	154	372	129	—190 G
11 days	2,550	11.2	50.0	49.1	170	340	133	—100 G
15 days	3,270	11.5	53.0	46.0	247	465	142	+370 G
15 days	2,930	9.8	49.0	49.5	167	342	117	

minus 2 by the total contents of the tube in cubic centimeters minus 2. The red cell per cent. is calculated from the hematocrit tube by dividing the red cell reading by the total hematocrit reading minus 2. The blood volume is divided by the body weight in kilograms which gives the blood volume in c.c. per kilograms of body weight and the percentage of blood to body weight is derived from

TABLE 3.—CHART C: OF THIRTY NEW-BORN INFANTS, BLOOD VOLUME ESTIMATIONS FROM TWO AND ONE-HALF HOURS TO FIFTEEN DAYS. GROUPED ACCORDING TO WEIGHT

Weight in Gm.	Age	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Pigment Volume	Hb.	Red Blood Cells	Weight Loss or Gain Before Blood Volume
2,550	11 days	11.2	50.0	49.1	170	340	133	306	90	4,290,000	—100 G
2,710	8 hrs.	8.1	41.3	56.5	193	469	173	483	103	.....	0
2,830	28 hrs.	12.5	38.4	61.5	169	441	157	467	106	7,200,000	— 70 G
2.880	24 hrs.	10.25	30.7	67.2	170	553	192	635	115	5,464,000	
2,890	10 hrs.	12.4	45.5	53.6	160	354	122	354	100	5,060,000	—120 G
2,890	9 days	10.7	41.5	57.5	154	372	129	405	109	4,660,000	—190 G
2,950	32 hrs.	10.6	41.5	57.0	137	331	112	307	93	4,648,000	— 80 G
2,950	49 hrs.	10.5	35.7	62.8	227	635	188	857	135	5,520,000	+150 G
2,980	3 hrs.	11.5	35.7	63.4	159	446	150				
2,980	5 days	12.0	42.5	56.75	192	454	152	444	98		
3,060	3 days	10.75	46.5	52.0	177	382	125	...	...	.....	— 90 G
3,150	3 days	9.8	42.9	56.0	156	364	116	382	105	5,644,000	— 70 G
3,160	36 hrs.	10.3	40.0	58.0	204	507	161	496	98	.....	—160 G
3,230	26 hrs.	8.8	37.5	61.5	142	378	117	359	95	.....	— 95 G
3,270	15 days	11.3	53.0	46.0	247	465	142	348	75	.....	+370 G
3,275	15 hrs.	11.75	37.8	59.5	136	361	110	393	109	5,140,000	
3,300	6 days	11.8	42.8	56.0	209	490	149	534	109	5,420,000	—100 G
3,350	2½ hrs.	8.6	36.0	61.6	184	513	155	523	102		
3,370	5 hrs.	11.4	34.2	63.0	184	540	160	615	114	5,730,000	
3,390	17 hrs.	10.8	51.9	46.3	188	363	107	304	84		
3,410	4 days	12.0	46.3	52.5	204	440	125	...	...	.....	— 10 G
3,470	24 hrs.	12.2	37.3	61.4	252	676	195	770	114	.....	—120 G
3,495	30 hrs.	11.3	28.0	70.5	152	542	155	672	124	6,480,000	— 65 G
3,560	48 hrs.	12.2	44.7	54.0	264	590	165	601	102	5,080,000	—185 G
3,620	32 hrs.	11.3	42.0	57.0	263	627	173	664	106	5,050,000	— 90 G
3,720	12 hrs.	11.2	43.7	55.3	245	566	153	549	97	5,552,000	—125 G
3,740	4 days	10.5	36.7	62.3	199	545	146	588	108	5,992,000	—110 G
3,860	12 hrs.	11.3	48.5	49.5	214	441	114	432	98	5,640,000	— 55 G
4,130	6 hrs.	11.75	31.0	67.0	202	595	144	702	118	5,096,000	
4,460	14 hrs.	12.25	33.0	65.3	283	857	192	899	105	.....	—170 G

this figure by simply pointing off one place. The pigment volume is obtained by multiplying the hemoglobin per cent. by the blood volume. This gives a valuable index of the curve of blood regeneration.

DISCUSSION

It is interesting to note the great variation of blood volume per cent. in new-born infants, which ranges from 10.7 to 19.5 per cent.

TABLE 4.—Eleven Fairly Normal Infants, Aged From Fifteen Days to One Year

Name	Diagnosis	Age	Weight, Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Hb., per Cent.	Pigment Volume	Reaction
B. O.	Normal	15 days	2,930	9.8	49.0	49.5	167	342	117	..	...	Temp. 38 C. then immediately normal, otherwise O.K.
	Normal	39 days	3.350	10.7	65 4	33.6	257	393	117+	63	247	Slight loss, O.K.
		50 days	3,560	10.8	67.5	31.5	279	413	116	52	214	No reaction
B. H.	Normal	4 mos.	5.070	9.0	61.2	37.8	357	582	115	61	354	No reaction
	Normal	4½ mos.	5,270	10.9	60.5	38.1	364	601	114	60	360	Temp. 38.4 C.,otherwise O.K.
		5 mos.	5,190	10.0	63 5	33.5	384	605	117	50	302	No reaction
		5½ mos.	5.560	10.4	65.5	33.6	420	640	115	..	...	No reaction
B. R. H.	Normal	9½ mos.	7,260	9.2	63.1	35.8	519	822	113	60	493	Temp. 39.4 C., loss 90 gm., O.K.
	Normal	10 mos.	7,470	12.3	65.8	33.3	543	825	110	52	428	Temp. 38 C., loss 30 gm., O.K.
B. S.	Hare-lip	4 mos.	4,940	11.7	65.75	32.5	387	589	119+	..	...	No reaction
	Cleft palate	4½ mos.	4,910	10.0	65.5	33.5	378	576	117+	..	...	Temp. 39 C., O.K.
		6 mos.	6.290	10.75	62 0	36.8	426	687	109+	59	405	No reaction
B. T.	Feeding case	10 mos.	6.120	8.5	62.4	37.0	371	595	97	..	...	No reaction
	Rickets	10¼ mos.	6,250	11.6	64.7	34.4	374	577	92	..	...	Temp. 39.2 C., vomited 9 times, O.K.
			6,300	9.8	68.4	30.6	400	585	93	..	...	No reaction
B. J.	Normal	2½ mos.	3.760	12.05	65 0	34.1	239	367	97	..	...	No reaction
	Normal	3 mos.	3,920	9.5	72.5	26.3	275	380	97	..	...	No reaction
B. V.	Spasmophilia	7 mos.	5.350	9.0	64.0	35.0	362	566	106	..	...	Loss 140 gm., O.K.
	Rickets	7½ mos.	5,600	10.55	66.0	33.2	361	546	97	..	...	Loss 40 gm., O.K.
B. B.	Eczema	11½ mos.	6.510	9.9	58.0	40.9	473	815	126	62	505	No reaction
		12 mos.	6,420	10.5	60.9	38.0+	494	811	126	57	462	Temp. 38 C., otherwise negative
B. L.	Hydrocephalus	7 mos.	4,650	10.9	62.8	36.2	339	538	116	..	...	13 minutes late; no reaction
		7½ mos.	4,710	11.0	62.4	36.8	363	581	123	..	...	No reaction
		8 mos.	5,000	10 6	63.6	35.9	364	572	114	..	...	Loss 50 gm., O.K.
B. W.	Feeding case	6 mos.	4,170	10.2	66.0	33.8	309	468	112	52	243	No reaction
		6½ mos.	4,320	11.0	66 0+	32.2	339	509	117	55	279	No reaction
B. N. B.	Birth palsy	10 mos.	7,800	12.2	65.5	34.0	465	710	91	..	...	No reaction
		10¼ mos.	7,900	9.75	65.1	33.8	466	714	90.3	..	...	No reaction
		11 mos.	7.980	9.1	67.5	31.3	614	908	114	..	...	Temp. 38.4 C., otherwise O.K.
		11¼ mos.	8,180	10.9	68.7	30.3	617	900	110	..	...	Temp. 40 C., otherwise O.K.

of body weight and from 107 to 195 c.c. per kilogram and the pigment volume from 304 to 899 c.c. The averages for these are: blood volume per cent., 14.7; blood volume per kilogram, 147 cc.; and pigment volume 521 c.c. Another one of the interesting variations is that found between plasma volume and red cell volume. The plasma volume per cent. is small as compared with the relatively high red cell percentage. These findings are fairly constant in the new-born during the first ten days. We can ascribe no reason for these wide variations beyond the fact that the blood during the first few days is undergoing a definite adjustment to its new surroundings. We know from studies on blood proteins and blood sugars, that a similar wide variation occurs during these first few days before the normal averages are established and the blood volume undoubtedly goes through this same period of adjustment when the blood forming organs are probably called on to function independent of any assistance from the maternal circulation. Of course it is not assumed that the blood forming organs have not been functioning throughout the fetal period but certainly during the first few days there must be some very definite adjustment to be established and it is therefore not surprising to find wide individual variations with rapid changes in accommodation taking place. We all know how easily blood changes occur during this period and how difficult it is for them to right themselves when any factor intervenes to disturb in any way the blood forming organs. There does not seem to be any constant correlation between blood volume and either weight, length or age in hours or days up to fifteen days.

In the infants tested who were from 15 days to 1 year of age, there is a very definite uniformity, constant at least for individuals and the variations between individuals are very much less marked than in the first fifteen days, the extremes being from 9.0 to 12.6 per cent. and the average 10.9 per cent. There seems to be a fairly definite attempt to stabilize the blood volume during the first few months and for any given infant over a period of several months at least the blood volume apparently remains at a fairly constant level as is shown in Table 4, except where some condition has intervened which might easily be assumed to have changed the blood volume.

In the pathologic cases changes from the normal blood volume are quite striking. We do not desire to discuss these variations at this

TABLE 5.—Of Three Infants With Fairly Marked Secondary Anemia

Name	Diagnosis	Age	Weight, Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Hb., per Cent.	Pigment Volume	Reaction
B. K.	Premature.....	12 mos.	6,420	11.0	75.0	24.0	378	504	78.5	..	...	No reaction
		12¼ mos.	6,520	10.6	77.0	22.7	373	485	74.5	25	121	Temp. 39.2 C., loss 70 gm.
		12½ mos.	6,780	9.5	79.5	20.0	418	525	77.5	25	131	Temp. 38.2 C., otherwise O.K.
B. F.	Premature.....	5½ mos.	3,080	10.9	72.0	27.0	216	300	97.5	52	156	Temp. 38.6 C.
		5¾ mos.	3,210	9.6	76.5	22.9	225	294	92.0	52	153	None
		6 mos.	3,280	10.2	80.2	18.6	230	288	87.5	..	...	Refused feedings for 2 days
B. C.	Premature.....	7½ mos.	3,550	11.9	73.1	26.0	233	318	89.9	45	143	Temp. 39.6 C.
		8¼ mos.	3,830	10.5	80.5	19.0	295	366	95.6	25	91.5	None; loss 60 gm.
		8½ mos.	3,860	10.55	82.5	17.0	351	425	110.0	20	85	Temp. 38.2 C. (otitis media)
		9 mos.	4,760	10.1	69.2	29.0	390	560	118.0	37	207	No reaction

time but hope to enlarge our number of studies in time in order to be able to form a more definite idea as to the factors which effect or produce these variations. Some points are, however, interesting enough to be emphasized. In B. K. (Table 5) the blood volume is very low, from 74.5 to 78.5 c.c. per kilogram of body weight. He was a typical fat, water-logged baby of the type so often seen which has been fed on a high carbohydrate diet. His plasma per cent., from 75 to 79.5, was very high in comparison with the other normal children of his age as B. N. B. who had a blood plasma of from 65 to 68.7 per cent. and a blood volume of from 90.3 to 114 c.c. per kilogram. B. F. and B. C. show the blood volume of quite marked secondary anemia so often found in premature infants. B. C., in addition, has as marked a clinical type of rickets as is often seen. Their plasma per cent. was also very high (from 69.2 to 82.5) and their red cell per cent. from 17 to 29, very low, as might be expected. In another case of severe anemia in an older child, not here reported, the plasma volume ran up to 85+ per cent. and the red cell percentage was 14.

While making these studies on blood volume, we have been struck by the practically uniform appearance of bile pigment in the serum of the new-born infants. The serum when pipetted off has a yellowish color. We have had several samples tested for bile pigment and in all bile pigments have been demonstrated.

Bang [10] found bile pigment in the blood obtained from the umbilical cord. He concludes that icterus in the new-born is a physiologic condition and the amount of pigment shows a constant increase in the blood after the first few days; he considers it only a question of degree between the new-born with or without icterus neonatorum. Our findings would corroborate Bang's findings. In many of our cases icterus, in so far as we were able to observe it, never appeared.

We are now making a more careful analytical study of this condition and hope to report on it in the near future. This undoubtedly has a distinct bearing on the appearance of certain of the hemorrhagic conditions of the new-born. In one of our babies which showed icterus almost from birth (it was observed when 4 hours old) bile pigment

10. Bang, F.: Jaundice of the Newly-Born, Hospitalstidende **8**:637 (June) 1915.

was present in very large amounts as shown by the marked discoloration of the serum when we made our blood volume determinations at 10 hours of age.

Thanks are due Dr. Whipple and Mrs. Robscheit for their many suggestions and valuable assistance on this report and on our further studies which are in progress.

We wish to thank Mr. Francis Smyth of the Hooper Foundation for Medical Research, who tested the samples for bile pigments, using the method described by Hooper and Whipple.[11]

11. Hooper and Whipple: Am. J. Physiol. **40**:332, 349 (April) 1916.

STUDIES ON BLOOD SUGAR—EFFECT OF BLOOD CONSTITUENTS ON PICRATE SOLUTIONS

A CONSIDERATION OF THE LIMITATIONS OF THE MODIFIED LEWIS-BENEDICT TEST *

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While working on a blood sugar problem we became interested in the statement of McLean [1] that "it is doubtful whether the picric acid method is at all reliable in the case of whole blood on account of the creatinin (and probably other interfering substances)" which under the conditions of the estimation gives a color similar to that produced by glucose in the presence of picric acid. De Wesselow [2] claims to show that the Benedict method with whole blood gives 45 per cent. higher readings than the McLean method which utilizes an entirely different principle—precipitation of protein with heat and dialyzed iron and a procedure which is thought to overcome the tendency to oxidation of cuprous oxid during titration.

We have done so much work with the Lewis-Benedict method, and it has been so satisfactory in our hands as a clinical test, that we decided to satisfy ourselves as to the correctness of these statements before giving it up as the routine method in the clinic.

The results of our investigation may be of interest. We have done the following experiments which may have some bearing on the reliability of the Lewis-Benedict test and which may give some added information concerning substances which appear in the blood under abnormal conditions that may influence blood sugar records and explain the occurrence of "hyperglycemia" without glycosuria.

The Effect of Oxalation.—Blood was drawn from four diabetics and one normal person. As quickly as the blood was drawn, 2 c.c.

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1. Maclean, H.: On the Estimation of Sugar in Blood, Biochem. Jr. **13**:135, 1919.

2. De Wesselow, C. L. V.: Picric Acid Method for Estimation of Sugar in the Blood and Comparison of This Method with that of Maclean, Biochem. Jr. **13**:148, 1919.

were placed in a volumetric flask, laked with distilled water and precipitated in the ordinary way with picrate solution. The blood was not oxalated. The analysis was carried through immediately. The remainder of the blood was oxalated and determinations were made by the Lewis-Benedict method one half hour later (Table 1).

This shows that oxalation produces no difference in the reaction.

The Effect of Creatinin.—We have shown by a simple gross experiment that creatinin added directly to a 2 c.c. sample of blood increases the blood sugar record given by the Lewis-Benedict method (Table 2).

TABLE 1.—EXPERIMENT 1. NOV. 12, 1919

Case	Nonoxalated Sample	Oxalated Sample
Labar	0.204	0.200
Cassel	0.175	0.170
Germain	0.200	0.200
Fregel	0.312	0.312
Kozolowski (control)	0.117	0.120

TABLE 2.—EXPERIMENT 2. NOV. 22, 1919

Control Blood 0.125%	2 c.c. Blood + 1 mg. Creatinin = 50 mg. per 100 0.180%	2 c.c. Blood + 2 mg. Creatinin = 100 mg. per 100 0.260%

These amounts of creatinin are many times greater than, probably, ever occur in blood in disease. The highest blood creatinin we find recorded is 33.3 mg. per cent. in a case of nephritis due to mercurial poisoning reported by Meyers and Killian.[3]

We next attempted to determine the lowest limit of sensitivity of the picrate solution to creatinin in water solutions and in blood (Tables 3 and 4).

In Series 2 of this experiment a distinct color change with a 2 c.c. sample of a creatinin solution containing 2.5 mg. in 100 c.c. of water is shown. In other words, the picrate solution is sensitive to 0.00005 gm. creatinin in water.

A distinct color change occurs in the picrate solution when 2 c.c. of a solution of 6 or 7 mg. of creatinin to 100 c.c. of water are added to a 2 c.c. sample of normal blood (Table 5). In other words, in

3. Meyers, V. C., and Killian, J. A.: Prognostic Value of Creatinin of the Blood in Nephritis, Am. J. M. Sc. **157**:674, 1919.

order that creatinin in the blood may have any influence on a Lewis-Benedict blood sugar record, it must be increased at least 6 or 7 mg. above normal which would give a creatinin value of 9 mg. per cent. or above.

TABLE 3.—EXPERIMENT 3. DEC. 29, 1919. CREATININ IN WATER. SERIES 1

Size of Water Sample	Creatinin		Blood Sugar Record, L.-B. Test
	Amount Added	Strength of Solution	
2 c.c. control	.....	.....	0.040
2 c.c.	2 c.c.	200 mg. in 100 c.c. water	0.333
2 c.c.	2 c.c.	190 mg. in 100 c.c. water	0.285
2 c.c.	2 c.c.	180 mg. in 100 c.c. water	0.270
2 c.c.	2 c.c.	170 mg. in 100 c.c. water	0.270
2 c.c.	2 c.c.	160 mg. in 100 c.c. water	0.270
2 c.c.	2 c.c.	150 mg. in 100 c.c. water	0.250
2 c.c.	2 c.c.	140 mg. in 100 c.c. water	0.250
2 c.c.	2 c.c.	130 mg. in 100 c.c. water	0.222
2 c.c.	2 c.c.	120 mg. in 100 c.c. water	0.225
2 c.c.	2 c.c.	110 mg. in 100 c.c. water	0.222
2 c.c.	2 c.c.	100 mg. in 100 c.c. water	0.222
2 c.c.	2 c.c.	90 mg. in 100 c.c. water	0.215
2 c.c.	2 c.c.	80 mg. in 100 c.c. water	0.220
2 c.c.	2 c.c.	70 mg. in 100 c.c. water	0.220
2 c.c.	2 c.c.	60 mg. in 100 c.c. water	0.182
2 c.c.	2 c.c.	50 mg. in 100 c.c. water	0.166
2 c.c.	2 c.c.	40 mg. in 100 c.c. water	0.143
2 c.c.	2 c.c.	30 mg. in 100 c.c. water	0.135
2 c.c.	2 c.c.	20 mg. in 100 c.c. water	0.090
2 c.c.	2 c.c.	10 mg. in 100 c.c. water	0.090
2 c.c. control	.....	.....	0.040

TABLE 4.—EXPERIMENT 3. DEC. 29, 1919. CREATININ IN WATER. SERIES 2

Size of Water Sample	Creatinin		Blood Sugar Record, L.-B. Test
	Amount Added	Strength of Solution	
2 c.c. control	.....	.....	0.040
2 c.c.	2 c.c.	60 mg. in 100 c.c. water	0.200
2 c.c.	2 c.c.	50 mg. in 100 c.c. water	0.160
2 c.c.	2 c.c.	40 mg. in 100 c.c. water	0.133
2 c.c.	2 c.c.	30 mg. in 100 c.c. water	0.111
2 c.c.	2 c.c.	20 mg. in 100 c.c. water	0.080
2 c.c.	2 c.c.	10 mg. in 100 c.c. water	0.070
2 c.c.	2 c.c.	5 mg. in 100 c.c. water	0.060
2 c.c.	2 c.c.	2½ mg. in 100 c.c. water	0.050
2 c.c. control	.....	.....	0.040

The remarkable sensitiveness of the picrate solution is better comprehended when we recognize the fact that in the 2 c.c. sample of blood, plus the creatinin solution, there is only 0.00016 gm. of creatinin present.

We have seen that the highest blood creatinin is 33.3 mg. per cent.[3] If the record obtained by this amount (0.045, Table 5) added to blood is added to a normal blood sugar record, $0.150 + 0.45 = 0.195$,

the upper border of normal is certainly reached. If, on the other hand, a case of diabetes was complicated by a marked renal disturbance inducing a high blood creatinin, one might expect a considerable increase in the blood sugar record not due to glucose.

TABLE 5.—EXPERIMENT 4. JAN. 2, 1920. CREATININ IN BLOOD. SERIES 1

Size of Blood Sample	Creatinin		Blood Sugar Record, L.-B. Test	Difference from Control Average
	Amount Added	Strength of Solution		
2 c.c.*	.....	.....	0.118	
2 c.c.	2 c.c.	190 mg. in 100 c.c. water	0.475	0.356
2 c.c.	2 c.c.	180 mg. in 100 c.c. water	0.330	0.211
2 c.c.	2 c.c.	170 mg. in 100 c.c. water	0.330	0.221
2 c.c.	2 c.c.	160 mg. in 100 c.c. water	0.320	0.201
2 c.c.	2 c.c.	150 mg. in 100 c.c. water	0.350	0.131
2 c.c.	2 c.c.	140 mg. in 100 c.c. water	0.222	0.103
2 c.c.	2 c.c.	130 mg. in 100 c.c. water	0.222	0.103
2 c.c.	2 c.c.	120 mg. in 100 c.c. water	0.224	0.105
2 c.c.	2 c.c.	110 mg. in 100 c.c. water	0.308	0.189
2 c.c.	2 c.c.	100 mg. in 100 c.c. water	0.247	0.128
2 c.c.	2 c.c.	90 mg. in 100 c.c. water	0.247	0.128
2 c.c.	2 c.c.	80 mg. in 100 c.c. water	0.243	0.124
2 c.c.	2 c.c.	70 mg. in 100 c.c. water	0.218	0.099
2 c.c.	2 c.c.	60 mg. in 100 c.c. water	0.221	0.102
2 c.c.	2 c.c.	50 mg. in 100 c.c. water	0.198	0.079
2 c.c.	2 c.c.	40 mg. in 100 c.c. water	0.165	0.046
2 c.c.	2 c.c.	30 mg. in 100 c.c. water	0.164	0.045
2 c.c.	2 c.c.	20 mg. in 100 c.c. water	0.140	0.021
2 c.c.	2 c.c.	10 mg. in 100 c.c. water	0.132	0.013
2 c.c.*	.....	.....	0.120	
Series 2				
2 c.c.*	.....	.....	0.110	
2 c.c.	2 c.c.	10 mg. in 100 c.c. water	0.141	0.030
2 c.c.	2 c.c.	9 mg. in 100 c.c. water	0.143	0.033
2 c.c.	2 c.c.	8 mg. in 100 c.c. water	0.127	0.016
2 c.c.	2 c.c.	7 mg. in 100 c.c. water	0.122	0.011
2 c.c.	2 c.c.	6 mg. in 100 c.c. water	0.118	0.007
2 c.c.	2 c.c.	5 mg. in 100 c.c. water	0.117	0.006
2 c.c.	2 c.c.	4 mg. in 100 c.c. water	0.117	0.006
2 c.c.	2 c.c.	3 mg. in 100 c.c. water	0.118	0.007
2 c.c.	2 c.c.	2 mg. in 100 c.c. water	0.111	
2 c.c.	2 c.c.	1 mg. in 100 c.c. water	0.108	
2 c.c.*	.....	.....	0.113	

* Control.

The Effect of Urea.—If 4 or 5 mg. urea crystals are added to a 2 c.c. sample of blood, a color change in the picrate solution may be obtained. This amount is far above the amount that ever occurs in the circulating blood. With graded and accurately measured amounts of urea, such as might occur as excess in circulating blood, no change in color whatsoever takes place (Tables 6 and 7).

Dilutions of urea in blood exactly like those tabulated for water were set up and run. There was absolutely no change produced by these amounts of urea.

From the above experiment it will be seen that in these amounts urea does not interfere.

Uric acid does not interfere. Ammonia nitrogen does not interfere.

TABLE 6.—EXPERIMENT 5. MAY 20, 1920. UREA IN WATER

Size of Water Sample	Urea		Blood Sugar Record, L.-B. Test
	Amount Added	Strength of Solution	
2 c.c. control	.....	.....	0.040
2 c.c.	2 c.c.	300 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	200 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	100 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	90 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	80 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	60 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	50 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	40 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	30 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	20 mg. in 100 c.c. water	0.040
2 c.c.	2 c.c.	10 mg. in 100 c.c. water	0.040

TABLE 7.—EXPERIMENT 6, MAY 20, 1920. UREA IN BLOOD

Size of Blood Sample	Urea		Blood Sugar Record, L.-B. Test
	Amount Added	Strength of Solution	
2 c.c. control	.....	.....	0.112
2 c.c.	2 c.c.	300 mg. in 100 c.c. water	0.113

TABLE 8.—EXPERIMENT 7. MAY 22, 1920. THE EFFECT OF URIC ACID

2 c.c. water control	0.040
2 c.c. water + 2 mg. uric acid	0.040
2 c.c. blood control	0.100
2 c.c. blood + 1 mg. uric acid	0.100

The Effect of the Amino Acids.—Glycocol: Two c.c. of water plus a knife point of glycocol. Boiling for ten minutes produces no change. On standing twenty minutes no change. After complete cooling one hour and fifteen minutes, consolidation in both tubes, the glycocol tube shows a definite change. After reheating for ten minutes the readings shown in Table 9 were obtained.

Tyrosin, taurin, tryptophan and alanin induce no change. These are all the amino acids we could find.

TABLE 9.—EXPERIMENT 8. EFFECT OF GLYCOCOL

2 c.c. water control	0.040
2 c.c. glycocol tube	0.190

The Effect of Epinephrin.—If a drop or two of epinephrrin solution (1 : 1,000) is added to picrate, Fehling's or Benedict's solution, a distinct reduction takes place. The experiments tabulated in Table 10 show the lowest limit of sensitivity of the picrate solution to epinephrin in water and in blood.

TABLE 10.—EXPERIMENT 9. EPINEPHRIN IN WATER

Size of Water Sample	Epinephrin		Blood Sugar Record	Water Control Record	Date and Remarks
	Amount Added	Strength of Solution			
2 c.c.	1.5 c.c.	1:1000 water	0.800	0.040	Dec. 5, 1919, open bottle
2 c.c.	2.0 c.c.	1:1000 water	1.000		epinephrin
2 c.c.	2.0 c.c.	1:1000 water	0.900	0.040	Dec. 8, 1919, new bottle
2 c.c.	1.0 c.c.	1:1000 water	0.450		epinephrin
2 c.c.	7 minims	1:1000 water	0.200		
2 c.c.	3 minims	1:1000 water	0.115		
2 c.c.	1 minim	1:1000 water	0.070		
2 c.c.	2.0 c.c.	1:1000 water	0.337	.....	March 27, 1920, epine-
2 c.c.	2.0 c.c.	1:2000 water	0.205		phrin had stood in
2 c.c.	2.0 c.c.	1:4000 water	0.148		corked bottle since
					Dec. 8, 1919
2 c.c.	2.0 c.c.	1:5000 water	0.125	.....	New bottle May 25, 1920
2 c.c.	2.0 c.c.	1:7500 water	0.111		
2 c.c.	2.0 c.c.	1:10,000 water	0.095		
2 c.c.	2.0 c.c.	1:20,000 water	0.075		
2 c.c.	2.0 c.c.	1:50,000 water	0.060		
2 c.c.	2.0 c.c.	1:100,000 water	0.040		
2 c.c.	2.0 c.c.	1:200,000 water	0.040		
2 c.c.	2.0 c.c.	1:400,000 water	0.040		
2 c.c.	2.0 c.c.	1:800,000 water	0.040		

The lowest limit of sensitivity in water is 2 c.c. of a 1 : 50,000 solution, or 0.00004 gm. The difference in the records obtained with the same dilution is explained by the condition of the sample, age, etc.

The experiment tabulated in Table 11 shows that epinephrin in infinitesimally small amounts induces a color change when added to blood. The lowest limit of sensitivity of the picrate solution of the Lewis-Benedict test to epinephrin added to blood is safely placed at 0.000025 per cent., or in other words, 0.025 mg. per cent. If we calculate the amount present in a 2 c.c. sample of blood plus 2 c.c. of a 1 : 4,000,000 solution, the picrate solution reacts to 0.0000005 gm. of epinephrin (adrenalin). From this it will be seen that the picrate solution is many-fold more sensitive to solutions of epinephrin added to blood than to water.

THE ACETONE BODIES

The Effect of Acetone.—Unless added in very large amounts, acetone in water solution produces no effect on picrate solutions. The acetone blows off. If acetone is added after heating the picrate and carbonate mixture a color change occurs with smaller amounts.

TABLE 11.—EXPERIMENT 10. APRIL 30, 1920. EPINEPHRIN IN BLOOD

Size of Water Sample	Epinephrin		Blood Sugar Record, L.-B. Test
	Amount Added	Strength of Solution	
2 c.c. control	.....	.....	0.127
2 c.c. control	.....	.....	0.120
2 c.c.	2 c.c.	1 mg. in 100,000 c.c. water	0.196
2 c.c.	2 c.c.	1 mg. in 200,000 c.c. water	0.171
2 c.c.	2 c.c.	1 mg. in 400,000 c.c. water	0.165
2 c.c.	2 c.c.	1 mg. in 500,000 c.c. water	0.153
2 c.c.	2 c.c.	1 mg. in 1,000,000 c.c. water	0.140
2 c.c.	2 c.c.	1 mg. in 1,500,000 c.c. water	0.138
2 c.c.	2 c.c.	1 mg. in 2,000,000 c.c. water	0.136
2 c.c.	2 c.c.	1 mg. in 2,500,000 c.c. water	0.135
2 c.c.	2 c.c.	1 mg. in 3,000,000 c.c. water	0.133
2 c.c.	2 c.c.	1 mg. in 4,000,000 c.c. water	0.130
2 c.c.	2 c.c.	1 mg. in 2,000,000 c.c. water	0.160
2 c.c.	2 c.c.	1 mg. in 1,000,000 c.c. water	0.176
2 c.c. conrtol	.....	.....	0.114

TABLE 12.—EXPERIMENT 11. DEC. 8, 1919. THE EFFECT OF PITUITARY EXTRACT

2 c.c. water control	0.040
2 c.c. water + 1 c.c. surgical pituitary extract (pituitrin)*	0.115
2 c.c. water + 1 drop surgical pituitary extract (pituitrin)	0.040
2 c.c. water + a few crystals of chlorbutanol	0.342
2 c.c. water + powdered pituitary gland (P. D.)	0.040

* Surgical pituitary extract (pituitrin) is put up in chlorbutanol. Pituitary extract induced no change.

TABLE 13.—EXPERIMENT 12. THYROID EXTRACT IN WATER

	Gm., Per Cent.
2 c.c. water control	0.040
2 c.c. water + 100 mg. powdered thyroid gland (P. D.)	0.100
2 c.c. water + 50 mg. powdered thyroid gland (P. D.)	0.080
2 c.c. water + 25 mg. powdered thyroid gland (P. D.)	0.060
2 c.c. water + 10 mg. powdered thyroid gland (P. D.)	0.040
2 c.c. water + 5 mg. powdered thyroid gland (P. D.)	0.040

The experiments summarized in Table 15 show the sensitiveness of the picrate solution to solutions of acetone added to the blood.

It will be observed that a distinct color change occurs in the picrate solution when a concentration of 2 c.c. of a solution of 0.05 mg. of acetone in 100 c.c. of water is added to 2 c.c. of normal blood. Placing

the normal acetone content of the blood at 1 or 2 mg. per liter,[4] or from 0.001 to 0.002 mg. per cent., we are safe in saying that acetone interferes in the Lewis-Benedict test when the acetone content of the blood is increased 0.05 mg. per cent. above normal.

TABLE 14.—EXPERIMENT 12. THYROID EXTRACT IN BLOOD

	Gm., Per Cent.
2 c.c. blood control	0.125
2 c.c. blood + 100 mg. powdered thyroid gland	0.200
2 c.c. blood + 50 mg. powdered thyroid gland	0.190
2 c.c. blood + 25 mg. powdered thyroid gland	0.166
2 c.c. blood + 10 mg. powdered thyroid gland	0.140
2 c.c. blood + 5 mg. powdered thyroid gland	0.130

Thyroid extract when added to blood induces a change.

TABLE 15.—EXPERIMENT 13. ACETONE IN BLOOD

Size of Blood Sample	Acetone		Blood Sugar Record, L.-B. Test			
	Amount Added	Strength of Solution	Series 1 May 1	Series 2 May 3	Series 3 May 4	Series 4 May 13
Control	.....	.....	0.113†	0.117‡	0.101§	0.103¶
2 c.c.	2 c.c.	*20 mg. to 100 c.c. water	0.250	0.210		
2 c.c.	2 c.c.	10 mg. to 100 c.c. water	0.230	0.195		
2 c.c.	2 c.c.	9 mg. to 100 c.c. water	0.230			
2 c.c.	2 c.c.	7 mg. to 100 c.c. water	0.198			
2 c.c.	2 c.c.	5 mg. to 100 c.c. water	0.185	0.180	.....	0.190
2 c.c.	2 c.c.	4 mg. to 100 c.c. wtaer	0.185	.....	.....	0.187
2 c.c.	2 c.c.	3 mg. to 100 c.c. water	0.180	.....	.....	0.193
2 c.c.	2 c.c.	2 mg. to 100 c.c. water	0.170	0.155	.....	0.189
2 c.c.	2 c.c.	1 mg. to 100 c.c. wtaer	0.150	.....	0.144	
2 c.c.	2 c.c.	0.75 mg. to 100 c.c. water	.....	0.140	0.143	0.172
2 c.c.	2 c.c.	0.50 mg. to 100 c.c. water	.....	0.135	0.135	0.170
2 c.c.	2 c.c.	0.25 mg. to 100 c.c. water	.....	0.125	0.128	
2 c.c.	2 c.c.	0.20 mg. to 100 c.c. water	.....	.....	0.127	0.144
2 c.c.	2 c.c.	0.10 mg. to 100 c.c. water	.....	.....	0.121	0.140
2 c.c.	2 c.c.	0.05 mg. to 100 c.c. water	.....	.....	0.114	

* Acetone C. P. dilutions based on specific gravity 0.797. Samples run with 100, 75, 50, 25, 15 and 10 mg. to 100 c.c. of water were practically black; no attempt was made to read them.
† Blood from a convalescent variola patient.
‡ Blood from a convalescent variola patient.
§ Blood from a normal person.
¶ The blood was taken from a boy who had an afebrile pyelitis

The remarkable sensitiveness of the picrate solution to acetone is better comprehended when we recognize the fact that in a 2 c.c. sample of blood to which is added 2 c.c. of a solution of 0.05 mg. of acetone to 100 c.c. of water, there is only 0.021 mg. (0.0000021 gm.) present.

4. "Normal blood when analyzed as described for total acetone bodies yields only 1 or 2 mg. of precipitate, equivalent to from 0.013 to 0.026 gm. of acetone per liter. In diabetes as much as 2.5 gm. (250 mg.) of acetone bodies, calculated as acetone, has been observed, while patients under ordinarily good control show from 0.1 to 0.4 gm." (per liter).

TABLE 16.—Showing the Comparative Sensitiveness of the Lewis-Benedict Test to Solutions of Glucose in Blood and Acetone in Blood

Size of Blood Sample	Mg. Added	Record Blood + Glucose, Mg. Per Cent.	Record Blood + Acetone, Mg. Per Cent.		Record Water + Glucose, Mg. Per Cent.	Difference Between Blood + Glucose and Control, Mg. Per Cent.
2 c.c.	100	0.202	0.250		.....	0.094
2 c.c.	75	0.168	0.230		0.070	0.060
2 c.c.	50	0.152	0.230		**0.053**	0.044
2 c.c.	25	**0.114**	0.198		0.040	0.006
2 c.c.	10	0.108	0.185		0.040	0.000
2 c.c.	5	0.102	0.185		0.040	
2 c.c.	4	.....	0.180			
2 c.c.	3	.....	0.170			
2 c.c.	2	0.105	0.150			
2 c.c.	1	0.104	0.140	0.144		
2 c.c.	0.75	.....	0.135	0.143		
2 c.c.	0.50	.....	0.125	0.135		
2 c.c.	0.25	.....		0.128		
2 c.c.	0.20	.....		0.127		
2 c.c.	0.10	.....		0.121		
2 c.c.	0.05	.....		**0.114**	0.040	
Control	.....	0.108 May 15	0.113 May 13	0.101 May 4	May 15-20	

Heavy figures show limit of sensitiveness.

TABLE 17.—Experiment 14. May 15, 1920. Glucose in Water

	Gm. Per Cent.
2 c.c. water control	0.040
2 c.c. water + 2 c.c. 100 mg. glucose – 100 c.c. water	Lost
2 c.c. water + 2 c.c. 75 mg. glucose – 100 c.c. water	0.070
2 c.c. water + 2 c.c. 50 mg. glucose – 100 c.c. water	0.053
2 c.c. water + 2 c.c. 25 mg. glucose – 100 c.c. water	0.040
2 c.c. water + 2 c.c. 10 mg. glucose – 100 c.c. water	0.040
2 c.c. water + 2 c.c. 5 mg. glucsoe – 100 c.c. water	0.040
2 c.c. water + 2 c.c. 2 mg. glucose – 100 c.c. water	0.040
2 c.c. water + 2 c.c. 1 mg. glucose – 100 c.c. water	0.040

TABLE 18.—Experiment 15. May 21, 1920. Diacetic Acid in Blood

Size of Blood Sample	Diacetic Acid		Blood Sugar Record, L.-B. Test
	Amount Added, Mg.	Strength of Solution	
2 c.c. control	...	.....	0.113
2 c.c.	100	Acetic-aceto-ester in 100 c.c. water	0.256
2 c.c.	80	Acetic-aceto-ester in 100 c.c. water	0.243
2 c.c.	60	Acetic-aceto-ester in 100 c.c. water	0.251
2 c.c.	50	Acetic-aceto-ester in 100 c.c. water	0.218
2 c.c.	40	Acetic-aceto-ester in 100 c.c. water	0.210
2 c.c.	30	Acetic-aceto-ester in 100 c.c. water	0.201
2 c.c.	20	Acetic-aceto-ester in 100 c.c. water	0.195
2 c.c.	10	Acetic-aceto-ester in 100 c.c. water	0.164
2 c.c.	5	Acetic-aceto-ester in 100 c.c. water	0.147
2 c.c.	5	Acetic-aceto-ester in 100 c.c. water	0.144
2 c.c.	0.75*	Acetic-aceto-ester in 100 c.c. water	0.128
2 c.c.	0.50	Acetic-aceto-ester in 100 c.c. water	0.127
2 c.c.	0.25	Acetic-aceto-ester in 100 c.c. water	0.115
2 c.c.	0.10	Acetic-acteo-ester in 100 c.c. water	0.115
2 c.c.	0.05	Acetic-aceto-ester in 100 c.c. water	0.113
2 c.c.	0.025	Acetic-aceto-ester in 100 c.c. water	0.112

* From this point on a different sample of blood was used. The record of the control reading was inadvertently omitted from the permanent record book. It was practically the same as the first control.

It may be of interest to show the comparative sensitiveness of picrate solution to solutions of glucose and solutions of acetone. Table 16 is compiled from previous experiments.

The picrate solution is sensitive to glucose in a concentration of 25 mg. per cent., to acetone in a concentration of 0.05 mg. per cent. Glucose water solutions give distinct color change at 50 mg. per cent. (Table 17).

TABLE 19.—EXPERIMENT 15. DIACETIC ACID IN WATER

Size of Blood Sample	Diacetic Acid		Blood Sugar Record, L.-B. Test
	Amount Added, Mg.	Strength of Solution	
2 c.c. control	...	.....	0.040
2 c.c.	100	Aceto-acetic-ester in 100 c.c. water	0.391
2 c.c.	80	Aceto-acetic-ester in 100 c.c. water	0.256
2 c.c.	60	Aceto-acetic-ester in 100 c.c. water	0.232
2 c.c.	50	Aceto-acetic-ester in 100 c.c. water	0.198
2 c.c.	40	Aceto-acetic-ester in 100 c.c. water	0.167
2 c.c.	30	Aceto-acetic-ester in 100 c.c. water	0.143
2 c.c.	20	Aceto-acetic-ester in 100 c.c. water	0.123
2 c.c.	10	Aceto-acetic-ester in 100 c.c. water	0.115
2 c.c.	5	Aceto-acetic-ester in 100 c.c. water	0.095
2 c.c.	4	Aceto-acetic-ester in 100 c.c. water	0.083
2 c.c.	2	Aceto-acetic-ester in 100 c.c. water	0.071
2 c.c.	1	Aceto-acetic-ester in 100 c.c. water	0.049

TABLE 20.—THE LIMIT OF SENSITIVITY OF PICRATE SOLUTION

	Gm.		Gm.
To glucose added to water is.....	0.001	Added to blood	0.0005
To creatinin added to water is.....	0.00005	Added to blood	0.00012
To diacetic acid added to water is.....	0.00002	Added to blood	0.00001
To acetone added to water is.....	.....	Added to blood	0.000001
To epinephrin (adrenalin) added to water is	0.00004	Added to blood	0.0000005

TABLE 21.—THE PICRATE SENSITIVITY IN BLOOD

To creatinin is approximately.....	4 times greater than to glucose
To diacetic acid is approximately.....	50 times greater than to glucose
To acetone is approximately.....	500 times greater than to glucose
To epinephrin (adrenalin) is approximately	1000 times greater than to glucose

The picrate solution used in the Lewis-Benedict blood sugar method is 500 times more sensitive to acetone than it is to glucose.

In these experiments the aceto-acetic-ester is hydrolyzed to diacetic acid and ethyl alcohol in the process of the test. The diacetic acid is unstable and rapidly decomposes into acetone and carbon dioxid. Ethyl alcohol also influences the picrate solution. We are safe in

making the statement that diacetic acid interferes when 0.25 mg. is added to 100 c.c. of blood or when 0.00002 gm. is added to a 2 c.c. sample of blood.

DISCUSSION

We have presented a series of experiments which tend to show that blood contains substances other than sugar which induce a color change in the picrate solution employed in the modified Lewis-Benedict blood sugar method. Under normal conditions, these substances may not interfere with the established normal range for this method. Under pathologic conditions several of these substances may interfere. Those which show the most marked influence are: epinephrin, acetone and diacetic acid. Creatinin may interfere, but does so in a less marked degree if we consider the comparative sensitiveness of the picrate solution to these substances.

As picrate solution reacts to smaller quantities of acetone than are normally present in the blood, the question may well be raised: do not the acetone bodies of the blood contribute to the established normal blood sugar range for the Lewis-Benedict test? Still another question may be asked: as epinephrin in infinitesimally small quantities induces a color change in the picrate solution, is it not possible that this substance when thrown into the general circulation, as is supposed to happen in emotional states, may induce a so-called hyperglycemia without mobilizing the glycogen stores of the liver?

DISCUSSION

DR. COWIE: The effect of heat on picrate solutions has been a matter of discussion. It is claimed by some workers that the longer the picrate solution is heated the more intense the color becomes. De Wesselow has obtained results which are the opposite of those obtained by Addis and Shevky. His experiment seems to show that with the continued application of heat there is a decrease in the depth of color. Our experience coincides with that of Addis and Shevky that up to a certain point, ten minutes, an increasing depth of color is produced. Thereafter up to thirty minutes the color change is permanent.

DR. SCHLOSS: I am extremely interested in what Dr. Cowie said about the Lewis-Benedict method inasmuch as I have used it for about nine years. I was particularly interested in McLane's criticism. It seems possible that under normal conditions the Lewis-Benedict is an essentially accurate clinical method, though it has a moderate error such as is present in any colorimetric method. I ran a series of observations using the Lewis-Benedict method and a control series in which the method of Bertrand was used. It is quite true the Lewis-Benedict method gave results constantly higher, but the difference was consistent and did not influence the results of observations made in normal cases. It is quite true, however, that a marked increase in creatinin will influence the results. The relationship of acetone and adrenalin are quite interesting, and should require a careful test of the accuracy of this method.

ACUTE CEREBROCEREBELLAR ATAXIA

WITH REPORT OF CASES *

J. P. CROZER GRIFFITH, M.D.

PHILADELPHIA

Five years ago I reported an instance of acute cerebellar ataxia, and reviewed the cases occurring in children, so far as examination of medical literature had brought them to my notice.[1] Since that time three other cases have come under my care. An occurrence as frequent as this, although undoubtedly dependent in some measure on coincidence, is certainly an indication that the disease is not as uncommon as we would suppose from the scanty reference to it in medical literature, and in most textbooks on diseases of children. The conviction of the existence of this apparently unsuspected frequency is the motive for the present communication.

Encephalitis is, as is well known, of not uncommon occurrence. In most cases, the large brain bears the brunt of the attack; but it is perfectly possible for the cerebellum to share in the process, or even to exhibit the chief symptoms. It is doubtful whether the process is limited to the cerebellum in any case. Certainly, as far as published case records go, symptoms pointing to involvement of the cerebrum also have always been observed. It is equally true that in the large majority of cases of acute hemorrhagic encephalitis cerebellar symptoms are absent.

What relation the lethargic encephalitis bears to other varieties of encephalitis is a matter which only time can solve, and cannot be discussed at length in this connection. The peculiar prominence of lethargy and asthenia seen in that disease is not characteristic of the majority of cases of other forms, and yet may occur in any of them, as S. Kinnear Wilson [2] pointed out. One of the instances of cerebellar ataxia which I have to report strongly suggests lethargic encephalitis.

REPORT OF CASES

Following are the histories of the four cases, with comments on them; the first case, already published, is abstracted for the sake of

1. Tr. Am. Ped. Soc. **27**:234, 1915; Am. J. M. Sc. **151**:24, 1916.
2. Lancet **2**:7, 1918.

completeness. In view of my former communication on the subject, any complete discussion of etiology and diagnosis would be repetition.

CASE 1.—Susie R., aged 5 years; negative family and personal history; was taken ill Jan. 4, 1915, with cold in the head and cough. Influenza was prevailing in Philadelphia at the time. The symptoms continued several days, the child being still out of bed. January 6, she was put to bed with fever and coated tongue. January 10, the temperature was normal, and the child was out of bed and apparently convalescent. January 12, vomiting occurred repeatedly; patient returned to bed complaining of pain in hip. She had now a jerking, irregular speech; the mind was clear. January 13, she was scarcely able to stand; irregular movements of eyes and eyelids; seemed dazed and later in day could not sit unsupported; attacks of screaming. Taken to the Children's Hospital January 14.

On entrance the mind was not entirely clear; speech very jerking and irregular, and only a few words could be said, and these with great difficulty. High degree of lateral nystagmus; knee jerks increased; decided incoordination of muscular movements; no fever. January 15, the mental condition was nearly normal; speech improved, but trembling; nystagmus marked; no paralysis; very decided ataxia of upper extremities. Could stand only when supported, and with feet far apart. Improvement went on very rapidly, and by January 23, nine days after admission to the hospital, could sit in bed unsupported. Nystagmus and ataxia of the arms were still present; some ataxia on standing, and the gait, when supported, showed apparent weakness and uncertainty. February 1, eighteen days after admission, there was still some difficulty in balancing herself when standing or walking; nystagmus was generally absent. The psychic condition had changed from sluggishness, haziness and dulness to alertness and brightness. The temperature has been afebrile while in the hospital. The examination of blood, urine and spinal fluid gave practically negative results.

Comment.—This case was an interesting instance of encephalitis involving apparently preponderatingly the cerebellum. That the cerebrum also shared in the process was indicated by the disturbed psychic state. The cause was not certainly discoverable, but there seemed good reason to consider influenza as the factor. An article by Heiman [3] discusses the subject of the relationship of encephalitis to influenza, as it applies to children, and reports a number of cases. None of them would appear to have been of the cerebellar type. At least, the presence of incoordination is not mentioned. Mills and Wilson [4] reported a case, probably dependent on influenza, and strongly resembling in some particulars that of Susie R.[4]

CASE 2.—Anna P., aged 4¾ years. Father said to have had a bad cough; otherwise the family history was negative. The patient had had no previous illness, except an attack of disturbance of the bowels and of whooping cough

3. Am. J. Dis. Child. **18**:83 (Aug.) 1919.
4. Arch. Neurol. & Psychiat **1**:567, 1919.

at the age of 2 years, and the mother thought she had not seemed entirely well since then. Two weeks before entering the Children's Medical Ward of the Hospital of the University of Pennsylvania, March 24, 1916, it was noticed that the left upper extremity seemed to have impaired power, and that she shook when she tried to use it. It was stated also that on one occasion she complained of being dizzy, staggered a little, and fell down the porch steps, but that she was not unconscious. That evening at the supper table she dropped her fork from the left hand. No more dizziness occurred; there had been no headache, and never any trouble in talking. The entire history of this sudden attack was rather vague. Apparently the first symptom was the momentary staggering and the falling down the steps, followed that evening by the ataxia of the arm. A day or two later the gait became uncertain, she "went to the left side when walking," and had to hold on to objects to keep from falling.

On admission to the hospital the patient was found well developed and well nourished; there was no paralysis of any extremity. The movements of the left hand were ataxic. The knee jerks were prompt, and no changes in other reflexes or in cutaneous sensibility were found. The patient stood with swaying and with the feet apart, and the gait was staggering, now to one side, and now to the other. There was no nystagmus, vomiting, or headache. Examination of the blood and urine on this date gave negative results. By April 1 the gait and station were much improved. The child could now stand without swaying, and could walk and even run without staggering. The ataxia of the upper extremity was unchanged.

Shortly after this date the patient developed scarlet fever and was removed to the Philadelphia Hospital for Contagious Diseases.

Nothing further was heard of her until brought at my request to my office, Dec. 29, 1919—three and three-fourths years after the attack. She seemed to be normal in nearly every way, except that there was distinct ataxic movement of the left hand in an effort to touch the tip of the nose, and slight swaying of the left arm in the effort to pick up a pin. On attempting to drink water from a glass held in the left hand, there was some tremor and unsteadiness. The mother thinks there is a slight dragging of the left foot when she tries to skip; but no difference in the movements of the two lower extremities could be detected at my examination.

Comment.—There would appear to have been no illness occurring immediately before the encephalitis developed, but it is possible symptoms really had been present but had not been observed. In any event, they could not have been severe. The suspicion of an unrecognized poliomyelitis of the ataxic form naturally arises, but, on the whole, this seems unlikely. The epidemic of that year had not commenced at the time; the early symptoms were almost too insignificant; the knee jerks were active, and there was no evidence under observation of any actual loss of power. Contrary to the condition of the first case, there was no nystagmus or affection of speech, and although these, it is true, are not characteristically cerebellar in origin, they are often associated with cerebellar disease. There was also no psychic disturbance. There was, however, a characteristic staggering gait and ataxia of the

arm. The condition described as a "lack of power" was without doubt an evidence merely of ataxia, since no loss of power could be detected on examination at the hospital. The "shaking" on attempting to use the arm may have been really a tremor, although there was none of this while under observation, but ataxia merely.

CASE 3.—Anna G., admitted to the Children's Hospital of Philadelphia, Nov. 22, 1916, aged 6 years. The family history was negative, and the previous personal history was unimportant until the occurrence of a very severe attack of measles, from which the patient suffered in July, 1916. From this she was supposed to have recovered completely; but the truth of this is questionable, since in August internal strabismus was noticed by the mother, and a little later it was observed that the child staggered when she walked. It was found, too, that she had become very backward and had difficulty in talking, and that at times she seemed to be dizzy. The symptoms were believed to be becoming worse.

Examination on admission showed the face blank and expressionless; decided mental apathy; very marked unresponsiveness; convergent strabismus; constant lateral nystagmus. The gait showed a tendency to go to the left, and the child to fall in this direction. There seemed to be no actual loss of power. Examination of the eyes by Dr. Shumway showed no lesions of importance. Spinal puncture gave a normal fluid. The reflexes were normal. The Baranyi test applied by Dr. Isaac Jones indicated a lesion of the upper posterior portion of the pons and the adjacent anterior superior portion of the cerebellum. An affection of the labyrinth was excluded.

December 5.—On this date, two weeks after admission to the hospital, there was little evidence of ataxia, but still distinct swaying when the eyes were closed. The child now walked well, but unsteadily. There was no ataxia of the arms.

The later history before she left the hospital showed a gradual improvement. The examination of the blood and urine gave no important results; the Wassermann reaction was negative; the von Pirquet faintly suggestive. The child talked but little to the physicians and nurses, but did to all the children, although her speech was slow and jerking. At one time a slight paralysis of the right side of the face seemed to be present, but this soon disappeared, and it was not certain that the observation was correct. The patient continued to be apathetic and to take little notice of her surroundings. The internal strabismus and the nystagmus and affection of gait persisted; but her mother, who saw her for the first time February 6, two and a half months after admission, thought that her eyes were a great deal straighter ,and that the improvement in walking and talking was remarkable. The child left the hospital the next day.

She was readmitted to the hospital Nov. 2, 1917, nine months after her discharge. The staggering gait had apparently for a time been recovered from, although the nystagmus still persisted. Three weeks previously she had commenced to vomit, at first occasionally and then daily; and she then commenced to stagger again. Examination showed the child with slight mental retardation; internal strabismus shifting from eye to eye; slight lateral nystagmus

of the left eye; the knee jerks were active but other reflexes normal. The principal complaint at this time appeared to be an inflammation of the tonsils and of the glands of the neck, from which she recovered in a few days. No further later history has been obtainable.

Comment.—The influence of the infectious diseases in producing encephalitis is well known. In this case there seems to be no question that the disorder followed an attack of measles. I have known this to occur in other cases. The inflammation clearly involved the cerebrum, as shown by the persistently affected mental state. That the cerebellum shared in the process seems equally indubitable. The combination of nystagmus and staggering gait leaves open scarcely any other conclusion.

CASE 4.—Alice W., aged 3½ years. Seen in consultation with Dr. Malcolm Council, April, 1919. The child had always suffered from chronic intestinal indigestion, and was of a highly neurotic disposition. Under careful treatment she had improved, although she was still subject to attacks from time to time, characterized by insomnia, accumulation of gas in the intestine, mucous stools, and increased nervousness. The family maintained that the child had grippe a short time before the attack of encephalitis which began April 2, 1919. On this day, without apparent reason, she vomited, became constipated, and then semi-stuporous, and her temperature rose to 100.5 F. On the next day, she had her first convulsion, and after this she had convulsive attacks at intervals of from 4 to 5 minutes, during which she stiffened and arched her back in the position of moderate opisthotonos. The attacks were of but a few seconds duration, and there was no rigidity at other times. During all this period she was in a very stuporous condition.

When seen by me the next day, April 3, there was persistent coma. Several of the convulsive attacks were observed, during which the child occasionally cried out. There was no taché; no rigidity, except during the convulsive moments, and no hyperpnea. The condition was supposed to be a toxemia of some sort, similar to that previously experienced, but with new and much more severe symptoms. On this account free purgation was advised, and enteroclysis with soda solution ordered.

I visited her again on April 5. The convulsive attacks had now ceased—they had lasted 60 hours in all—and the bowels had been freely purged; but the mental condition was unchanged; coma had continued, and no word had been spoken. Fever had persisted, the temperature reaching 102 F. The pulse was slow, hard and full. Inasmuch as the symptoms slightly suggested a meningitis, a lumbar puncture was made, but the fluid obtained was clear and absolutely sterile. There was still an entire immobility and absence of speech, and the child was usually much relaxed, with features somewhat sunken, and with occasional slight cyanosis. Most of the time the child was disposed to sleep, and even at the best was more or less soporose. April 8: There had been decided improvement, the patient having become fretful and restless. Although much of the time soporose, it was possible to rouse her and to arrest her attention for a moment.

Recovery advanced very slowly. The child did not speak at all for five months, and then began to say a few words such as "boy," "cow," "yes," and

the like. She slowly regained the power of voluntary movement, moving first the arm, and later rolling the head. As muscular movements increased there was a remarkable degree of incoördination noted, all movements being entirely undirected. It was late in August, 1919, before she walked perfectly and talked well, although even then speech was slow. A year after the attack she showed further improvement, but still talked slowly.

Comment.—The cause and nature of this case are not entirely clear. The family lived in the country, and the patient had not been in association with other children. There had been no illness in the house. At the same time it is to be noted that the affection occurred toward the close of the epidemic of influenza in 1918-1919, and that the family are confident that she had had an attack. It is also noteworthy that the symptoms bear in many respects a very decided resemblance to those of lethargic encephalitis, the coma, immobility, and asthenia being very striking features, although there was no evidence of paralysis of any of the cranial nerves. Whether or not the case is to be included in this category is uncertain, but it seems to be very probable. The condition suggests in some respects the cases of epidemic stupor described by Batten and Still,[5] their four cases exhibiting early and persistent stupor, and during convalescence a slow, hesitating speech.

The interesting feature is, that in addition to the involvement of the cerebrum, which was by far the most marked, very decided incoordination was observed during convalescence, pointing to an involvement of the cerebellum as well.

CONCLUSIONS

The conclusions to be derived from the cases now reported, and from those previously collected from medical literature, may be formulated as follows:

That there is a condition not common, but still certainly more frequent than ordinarily supposed, in which an acute hemorrhagic encephalitis involves the cerebellum, and which could be designated "acute cerebellar encephalitis."

That with this are always combined symptoms indicating an involvement of the large brain as well, and the title "cerebrocerebellar encephalitis," or "cerebrocerebello-bulbar encephalitis," is consequently to be preferred. The degree to which the process involves one or

5. Lancet **1**:636, 1918.

another part of the brain varies with the case; in some instances the cerebellar lesions predominating, in others the cerebral; but in all in the category of cerebellar encephalitis there is, as stated, a combination of the symptoms affecting both regions. In very many more instances the cerebellum escapes entirely, so far as symptoms indicate; but to these no reference is made here.

The cause of this cerebrocerebellar encephalitis varies decidedly. In the majority of the cases previously reported in medical literature, some infectious disease had preceded the attack. This was true of two of my own cases, but no such connection could be discovered in the other two. Among the symptoms oftenest to be seen are:

1. Unconsciousness, usually of but short duration, although this was observed in but one of my own cases.

2. Ataxia, a constant symptom in all instances.

3. Affection of speech, shown sometimes as a complete inability to speak which may last for months; in other cases manifestly an ataxia of speech rather than a mental disturbance. More or less involvement of speech was present in three of my four cases.

4. Disturbance of mentality, apart from unconsciousness, is seen in many instances. It was present in three of my cases. It is usually temporary, but may be very persistent.

5. Nystagmus was observed in two of my cases, and has been reported in a number of others. It is an interesting confirmatory symptom when it exists, but would appear oftener to be absent.

6. "Loss of power" is often a very evident symptom, at least in the observation of the families. It is, however, usually absent, and is probably nearly always dependent in reality on an ataxia. In a few instances, as in my fourth case, there has been a decided hypotonia for a time.

7. Active tendon reflexes are often observed. The knee jerks were increased in two of my four cases, and active in one.

Among other symptoms may be mentioned vertigo, which is conspicuous by its absence. However, the early age at which the majority of cases occurred rendered the determination of the existence of vertigo difficult. Two of my patients had complained of feeling dizzy. Whether this was actually vertigo or not is uncertain.

The consideration of the prognosis is of interest. As far as life is concerned it would appear to be good. Only one of the patients in

my first report died, and that was years later. This has prevented an exact study of the pathologic lesions. That the patients will not have clinical evidences of the disease persisting is, however, always uncertain. My first patient recovered absolutely; the second was left with a slight incoordination persisting more than three years after the attack; the third exhibited nine months later slight mental retardation and some remains of the cerebellar symptoms; the fourth had apparently recovered four months later, except that speech was still slow. It is possible that final disappearance of all symptoms may take place in all of them, inasmuch as in a case reported by Taylor [6] there were still symptoms discoverable three and one-half years after the attack, but none twenty years later. Of the seventeen cases collected from medical literature in my earlier report, complete recovery is known to have taken place in a considerable number, and it is probable that this was true of a number more. So far as statistics go, it would appear that the disease will leave no traces in the majority of instances.[6]

DISCUSSION

DR. HOWLAND: I should like to ask Dr. Griffith why he speaks of hemorrhagic encephalitis. I ask this question for information as to the pathological process. We have all seen patients with encephalitis for years. Most of them recover. There is always the question as to the character of the lesion. I have seen but two cases at necropsy that were considered to be examples of hemorrhagic encephalitis and both of these had hemorrhages as the result of thrombosis but not of encephalitis.

DR. RAMSEY: What were the results of lumbar puncture and what did you find in the cerebrospinal fluid?

DR. GRIFFITH: I referred to this condition as hemorrhagic encephalitis merely because textbooks on neurology usually designate it by this title, in contrast to the suppurative form. I have, however, never been thoroughly convinced that the title is a very good one. In answer to the question concerning lumbar punctures, I can say that this was done in all of my cases, and in all the results were entirely negative.

6. Lancet **2**:1416, 1904.

THE SIGNIFICANCE OF XANTHOCHROMIA OF THE CEREBROSPINAL FLUID

WITH REPORT OF A CASE IN A PREMATURE INFANT*

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This case is reported because of the occurrence of yellow spinal and ventricular fluid in an infant of eight months period of gestation who lived thirty-seven days and who also manifested marked internal hydrocephalus, pyelitis and bronchopneumonia. In the literature the term xanthochromia covers a variety of cerebrospinal fluids with different properties. Some insist that this name should be applied to yellow fluids which coagulate *en masse,* as Froin first described. Others reject the term xanthochromia when applied to fluids containing red blood cells. They propose the term erythrochromia for this condition. Our case was one of yellow cerebrospinal fluid containing red cells due to subpial hemorrhages. Because of the confusion and lack of agreement concerning our chief interest in this case, we will be obliged to interpret our conception of the condition called xanthochromia in order to present intelligently the findings.

The common properties of all xanthochromic fluids are yellow color and increased globulins. After these have been eliminated, the other considerations such as massive coagulation, pellicle formation, cell count and the presence of erythrocytes, are variable factors. The syndrome of xanthochromia most frequently mentioned is Froin's, or the complete syndrome which includes yellow color, massive coagulation and increased globulins. The cell count varies. Some include and others disregard the cells in their discussions because they have not analyzed their significance. It seems unnecessary to mention increased globulins where coagulation occurs, because coagulation without an increase in albumen is inconceivable. As a matter of fact, fluids with xanthochromia all have increased globulins, although the quantity may differ. Nonne has described what is now termed the incomplete syndrome, that is, yellow color with increased globulins, although massive coagulation does not occur. There seems to be considerable evidence, as we shall see later, that Nonne's is an earlier

or less complete development of Froin's syndrome. In general, it has been pointed out that the French emphasize the coagulation feature, while the German school speaks of the increased globulins, not mentioning the presence or absence of coagulation.

The whole situation resolves itself into the question of what causes the yellow color. Ultimately, the yellow pigment is hematogenous in origin. Mix [1] states that the pigment has been identified as hemolytic biliary pigment by Donath, as bilirubin by Blanchetriére and Lejonne, and as urobilin by Fornaca. Raven suggests that the color, in the last analysis, is due to blood pigment from multiple small hemorrhages because in his 47 cases, the yellow color was caused by an old hemorrhage. His conclusions hold only so far as those cases are concerned. Other causes must be assigned where no demonstrable hemorrhage is present. However, his opinion is confirmed by the case of Blanchetriére and Lejonne, a vascular cord tumor with multiple hemorrhagic foci. There were only a few red cells in the fluid, and they suggest that there were small continuous hemorrhages from the tumor over a period of sixteen months. All these cases might be classed as erythrochromic so far as the presence of red cells is concerned. There are other views concerning the pigment which refer particularly to the other types of xanthochromic production. Gordon [2] remarks that the pigments accumulate in greater concentration where there is a limited area for absorption as in a culdesac or in the cutting off of the spinal subarachnoid space in hydrocephalus. Inasmuch as absorption from the spinal subarachnoid space is all by way of the blood stream, and this course is closed by compressions and inflammations, as in the complete syndrome of xanthochromia, the pigment will have to accumulate in the meningeal pouch so formed. Thus, Raven, on the one hand, explains the yellow color on the basis of hemorrhage entirely, and Gordon, on the other, takes into account only the compression syndrome. Both are xanthochromic fluids, although the former may be termed erythrochromic and the latter the true Froin syndrome with the absence of red cells.

Instead of considering the other properties of xanthochromic fluids separately, we shall find that they can all be explained in a discussion of the pathogenesis of yellow color itself. This will simplify the problem and permit a more lucid presentation of the subject itself.

1. Mix: Surg. Clin. **4**:317, 1915.
2. Gordon: Canad. M. A. J. **9**:1005. 1919.

The most usual form of xanthochromia is that associated with compression of the spinal cord. Since first described in 1903, a large number of cases have been reported in the literature. Derrien, Mestrezat [3] and Rogers claim they were the first to point out the importance of the formation of a meningeal pouch in the production of xanthochromia. Siccard and Descomps were among the first to call attention to this fact, although they were wrong in their idea that the syndrome always spelled meningitis and never tumor. Indeed, since their time, most of the cases reported are cases of tumor. Everyone who has written on the subject has agreed to the importance of the pouch formation, and only recently Ayer [4] published some experimental work on the production of xanthochromia by compression produced by injecting paraffin into the spinal canal.

The obstruction may be produced by tumor, meningeal adhesions and trauma. The tumors may be of the ball-valve type, as Mix points out, and this will explain the variability of fluid findings which occur in some cases. Mestrezat showed that a transudate occurs into the meningeal pouch. In a closed cavity of this sort the elements necessary for xanthochromia and massive coagulation could come in two ways, as Horrax [5] states, either by transudation or by capillary hemorrhage the origin of which is not so clear although a few cases are reported with cord tumors. Mestrezat concludes that the physical and chemical properties of the fluid, together with the clinical and necropsy findings, demonstrate that a closed cavity and stasis of the fluid is necessary to the production of the syndrome. Therefore, there must be a closed cavity in which there accumulate the elements from the blood by transudation or hemorrhage, and, second, an alteration in the vessel walls of the cavity, either infectious or toxic, permitting the process to occur. It is usually a transudate. There is diminished pressure in the culdesac because the spinal fluid above the compression is shut off. The veins are dilated at the compression so that it is easy for transudation to occur. There is a high albumin content, and thrombin and fibrinogen also pass out. Mix states that these are the most characteristic constituents. Coagulation may occur in the needle itself, but sometimes it takes as long as a few hours to occur. The clot separates out from the fluid as a blood clot

3. Mestrezat: Thesis Paris, p. 425, 1912.
4. Ayer: Arch. Neurol. & Psychiat. **2**:158 (Aug.) 1919.
5. Horrax: Arch. Int. Med. **17**:632 (June) 1916.

behaves. He points out that the fibrin content runs close to the amounts found in the blood. Hanes [6] states that the high content of xanthochromic fluids in fibrin and proteids and the presence of a few cells support the view that real blood comes with the transudate, which is perfectly analogous to pleural transudates due to venous compression.

What determines the presence or absence of cells and what is their significance? Although we discussed the compression from the standpoint of the tumor, it is readily seen that the same symptoms might be produced by an inflammatory mass or traumatic process. In these cases the cell count is increased. Indeed, some authors suggest that an increased cell count differentiates tumor from inflammatory processes. Sprunt and Walker,[7] however, show that in seventeen of fifty-one cases of tumor the cell count was increased, and in one of their cases, a cord tumor, there were 61 mononuclear cells.

The formation of a pellicle is to be expected where there is a meningitis with insufficient compression to cause massive coagulation. It may also occur in the early stage of a tumor. Cooper [8] describes a case of angiosarcoma of the cord which showed edema of the membrane below the point of construction from which yellow fluid was withdrawn. A cobweb-like coagulum formed when the fluid was allowed to stand. There were no cells, and the globulins were increased.

The total absence of coagulation may also be explained. In the compression type of case it is a matter of duration of the process and the completeness and extent of the compression. Ayer [9] states that the most important variation gives a fluid which superficially does not seem to have any relation to the complete syndrome. Where presumably the pressure on the cord has been insufficient to shut off the spinal fluid we find a fluid of normal appearance, colorless, under normal pressure, but containing an abundance of globulins. This fluid does not clot and may not contain cells. Such a fluid corresponds more closely to Nonne's incomplete syndrome. As a variation from this the yellow color may be present. Hanes attempts to prove that Nonne's is only an earlier stage of the same process that gives Froin's syndrome. However, it may as well be a question of extent of

6. Hanes: Am. J. M. Sc. **151**:66, 1916.
7. Sprunt and Walker: Johns Hopkins Hosp. Bull. **28**:80, 1917.
8. Cooper: J. A. M. A. **55**:2298 (Dec. 30) 1910.
9. Ayer: Med. Clin. **1**:1143 (Jan.) 1918.

obstruction as duration. Hanes states that the complete syndrome may never be reached, but that the yellow color, increase in proteins and cells may be the only evidence of cord compression. What has been said regarding cell increase should be recalled here. Nammack [10] recently reported his observations on 5,801 spinal punctures. He quotes the ninety-two cases of tumors and other chronic surgical conditions of the cord by Elsberg and Rochefort [11] in which there were twelve fluids with xanthochromia, seven of which gave the complete syndrome. Of his own cases there were ninety-six, or 1.6 per cent., of yellow spinal fluids. In only six of his cases was the complete syndrome found. Yellow fluids occurred in two-thirds of his cases of tuberculous meningitis. He concludes that the smaller incidence of the complete syndrome in his cases was another indication that the earlier stages showed the Nonne syndrome, inasmuch as all his cases were acute or subacute affections. Incidentally, he remarks that a patient with meningeal symptoms and yellow fluid should be suspected of either tuberculosis or poliomyelitis. It may not be quite fair to include such cases of Nammack's with causes of cord compression because in the infections the factor of hemorrhage may play an important part. Blood cells are frequently found in tuberculous meningitis, and it is questionable whether hemorrhage alone gives the complete syndrome. The question of hemorrhage and its relation to xanthochromia we will consider separately. So far we have described the formation of yellow color, bringing in the explanations for massive coagulation, pellicle formation, cell increase and absence of coagulation.

The second type of process which gives xanthochromia without demonstrable compression phenomena is the process of continuous or multiple capillary hemorrhages. The compression phenomenon applied particularly to cord processes, although in Hane's case of a 9 months old child a tuberculous mass obliterated the pia arachnoid and completely encased the medulla at the level of the foramen magnum. The ventricular fluid was clear, but the spinal fluid presented the complete Froin's syndrome. The group we will now consider includes those cases of inflammation, neoplasms and trauma associated with red cells in the cerebrospinal fluid. The color of the fluids is due to dissolved hemoglobin or its derivatives, and they do not coagulate, as a rule. Because of the presence of erythrocytes some propose the name erythrochromia and place them in a separate category.

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10. Nammack: Am. J. M. Sc. **159**:540, 1920.
11. Elsberg and Rochefort: J. A. M. A. **68**:1802 (June 16) 1917.

There are many cases in the literature illustrating the occurrence of yellow spinal fluid with conditions permitting the slow escape of blood. In 1904, Cestan and Ravaut published a case of pachymeningomyelitis of the conus. They considered two factors in the production of the complete syndrome, first, a meningeal inflammation with a sero-fibrinous exudate and, second, hemorrhage with solution of the red cells in the fluid with the appearance of the yellow color due to freeing of the hemoglobin. These two factors may coexist. In fact, Babinski regarded the syndrome of Froin as being due to a fibrinous hemorrhagic meningitis.

Another type of process recalls the case of Blanchetriére and Lejonne to which reference has already been made. This was a vascular cord tumor of the small round cell type which contained many hemorrhagic foci. There were only a few cells in the fluid, and they accounted for the yellow color on the hypothesis that small continuous hemorrhages had occurred over a period of sixteen months. In Raven's forty-seven cases the spinal fluid was stained by the hemoglobin derivatives from old hemorrhages. Rindfleisch, in 1904, had three cases of metastatic sarcoma of the brain and cord. In two the fluid was once dark golden brown while at another time the fluid was clear yellow. This expresses well the relation of erythrochromia to xanthochromia, if such a distinction is desired. The sediment contained erythrocytes and large cells with large nuclei, probably endothelial cells, and the proteins were increased. Section of the tumor showed hemorrhagic foci. Dufour, in 1905, described a case of diffuse sarcomatous meningitis with yellow fluid containing many lymphocytes, a few erythrocytes and several makrocytes. He states there was no bleeding in this case. Not all blood containing tumors give rise to red cells in the fluid. In 1906, Grund described a case of gliosarcoma of the spinal cord with yellow fluid but no cellular elements. The spectroscope showed no blood although the tumor was full of the blood and extended to the meninges. In 1907, Erb reported a case of carcinoma of the cervical vertebrae with yellow fluid but no blood. In 1911, Heilig reported cases of "erythrocyte pigmentation" of the spinal fluid.

Tuberculous meningitis often, if not usually, shows red cells in the spinal fluid when associated with xanthochromia. Reich [12] described a case of tuberculous meningitis in which the fluid was of

12. Reich: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**:721, 1913.

a light bloody color but became a golden brown after centrifuging. In the sediment there were many erythrocytes, lymphocytes and an occasional polymorphonuclear leukocyte. Necropsy showed a hemorrhagic condition. He concludes that not only in tumors, but in cerebral hemorrhagic conditions yellow color of the spinal fluid may be found.

Xanthochromia with red cells is not limited to the conditions so far discussed, namely, Babinski's type of fibrinous hemorrhagic meningitis, cord tumors and meningitis of tuberculous and purulent origin. There is a wealth of evidence pointing to the responsibility of conditions within the cranial cavity in the production of the combination of yellow color and red cells. Tuffier reports cases of yellow fluid in skull fractures. Another case is cited of a patient who was ready to be operated on for brain tumor. The patient died, and at the necropsy a diffuse cerebral hemorrhage was found. In one of Rindfleisch's cases a brownish blood coagulum was seen in the fluid, and in this case there was a tumor mass adherent to the inner side of the lateral ventricle. In one of Erb's cases there was a hemorrhagic glioma on the right side of the brain. In this case, the first puncture yielded a clear fluid, but the second puncture showed red cells, polynuclear leukocytes and lymphocytes. These characteristics continued for some time. Further evidence of the cranial origin of the hemorrhage is furnished by Horrax's case. He reports the case of a boy aged 12 years, with a tumor of the pineal gland. The spinal fluid was straw colored, cloudy, and contained 1,011 old, disintegrating red cells and eighty-five white cells. There was no massive coagulation although the globulins were increased. From the ventricle of the same case 50 c.c. of yellow fluid with 561 old red cells and seventeen lymphocytes was obtained. Horrax states that many tumors grow into the ventricles accompanied by xanthochromia doubtless due to the escape of red cells from the surface of the tumor into the fluid. He reports having seen a number of such cases in his clinic. Sprunt and Walker hold that it is generally recognized that yellow color may occur in the spinal fluid after ventricular hemorrhage or hemorrhage into the subarachnoid space when the cells have disappeared almost entirely. They reviewed 100 cases from the literature and stated that there are some exceptions to the syndrome that cannot be explained on the basis of compression and obstruction. These usually vary from the complete syndrome in some particulars. Among the

cases unexplainable on the theory of compression is a group of brain tumors in contact with the meninges in which the yellow color and other abnormalities could be explained by small hemorrhages into the subarachnoid space. In these cases, they state, there are crenated blood cells or positive tests for hemoglobin. To the number of cases we have already quoted in support of this view, they add a case of endothelioma of the dura in the left middle fossa and a case of arteriosclerosis, chronic diffuse nephritis and arterial hypertension with hemorrhage into the lateral ventricles.

Hanes attaches considerable importance to the condition he calls erythrochromia and sharply distinguishes this from xanthochromia. According to him, the name erythrochromia would have to be applied to any xanthochromic fluid containing red cells. This would necessitate a division of yellow fluids which would hardly be justified on etiologic or pathologic grounds as the cases we have described would indicate. We do not wish unduly to emphasize the hemorrhage factor and we are inclined to agree with Sprunt and Walker that it is not necesary to presuppose minute hemorrhages to explain the color of the fluids in which there are no red cells and in which the most delicate tests for hemoglobin derivatives are negative and no bands appear in the spectrum. From the large amounts of fibrin and globulin it is evident that considerable transudation of blood plasma must have occurred. However, we think that certain conditions associated with hemorrhage have a definite place in the causation of xanthochromic fluids and cannot agree to a separation simply on the presence or absence of red cells. Essentially, the same process and origin of yellow fluid exists in both types. The process may better be understood if the whole question is simplified by classifying the conditions producing xanthochromia rather than to separate the syndrome on the grounds of more or less accidental variations in the fluid.

Hanes states that erythrochromic fluids are due to hemorrhage into the cerebrospinal fluid from ventricular apoplexy and traumatic rupture of meningeal vessels. We have already referred to cases of brain and cord tumors and cases of fibrinous and tuberculous meningitis giving red cells. He says that the color varies from bright red to a dark yellow and changes from day to day. Sprunt and Walker also state that in their experience the fluids containing hemoglobin are dark and have an amber tint, whereas those giving negative tests are of a lighter buff yellow. However, one of Froin's cases varied from

cherry red to red, reddish yellow, light yellow to absolute limpidity. Nine punctures were made from the first to the twenty-first day of the illness. The red cells were present in diminishing numbers, and serum albumin and globulin were present in varying amounts. The spectroscopic evidence of hemoglobin disappeared some time before the fluid became colorless.

A case cited by Siccard and Descomps showed red cells in the serum and in the clot that formed almost immediately in a xanthochromic fluid. A second puncture six days later was yellow and clear, and a third, twenty-three days after the first, was entirely clear.

The mere presence of red cells does not take the fluid out of the category of xanthochromia where the fluid is really yellow. In fact, the red color, although not a genuine xanthochromia, may precede the yellow color in point of time and probably is due to continuous hemorrhage. Gordon agrees with this conception, for he states that in many cases of xanthochromia there are either free red cells or the evidence of chemical blood. In others there is no chemical evidence of hemoglobin, but he concludes, as we have already mentioned, that there is no evidence that the pigment is other than the normal pigment of the blood plasma. In this connection let us again recall Rindfleisch's two cases of metastatic sarcoma of the brain and cord. The fluid in these cases was once dark golden brown while at another time it became clear yellow.

Hanes points out that another differentiating point is the constancy of the color in xanthochromia, but Siccard and Descomps have described the presence of xanthochromia and massive coagulation on some punctures and not on others. In Dimolet's [13] case, the first flow of yellow color actually changed to normal during the course of a single puncture. Sprunt and Walker cite a case in which a second puncture, performed three weeks after the first, yielded a clear yellow fluid with very faint globulin tests, and this at a time when the symptoms of compression were more marked.

The fluid may have the color of arterial blood and red cells or their shadows are found. In the minute type of hemorrhage, there will be no red color at all, and red cells have been found in fluids which were decidedly yellow and not contaminated with blood macroscopically.

13. Dimolet: Rev. Neurol. **22**:648, 1914.

Another objection to the red cells is based on the statement that leukocytosis of the fluid develops because of the meningeal irritation by the products of red cell destruction. However, in Horrax's case the ventricular fluid contained 561 red cells and seventeen lymphocytes. More white cells and more varieties should be expected. It is not denied that leukocytosis may occur, as in the case of Schwartz that Hanes quotes in his contention, but this is not a constant or characteristic part of the hemorrhage. It may be due to the infection producing the meningitis.

The fact that xanthochromia shows no red cells, and that there is neither chemical or microscopic evidence of hemoglobin derivatives is contradicted by Froin's first case, in which red cells were present, and Reichmann's report that he has often found the syndrome in cases of tumor of the brain and cord with yellow spinal fluid and multiple hemorrhages.

REPORT OF CASE

Our case belongs to the second type of yellow fluids, that is, the type not associated with compression but occurring with a process allowing blood to escape into the cerebrospinal fluid.

The infant was a premature baby, born during the eighth month of gestation. The mother had influenza and pneumonia. The child was brought to the hospital as a feeding case. The admission history stated that the child was apparently well at birth and the labor was not difficult. The father was well. Two maternal aunts had tuberculosis, and one died of the disease. The mother of the baby had frequent attacks of bronchitis, but the family physician stated that the process was not tuberculous.

On entrance the temperature was 95 F., and the child weighed 3 pounds 14 ounces. The child was placed in an incubator, and the temperature rose to 98.6 F. the next day. Breast milk was given by gavage, and occasionally skimmed milk was given during the stay of thirty-four days. The weight steadily increased to 5 pounds 2 ounces. After a few days of subnormal to normal temperature, it tended to rise so that it frequently reached 102 F. during the first ten days of life. This was not deemed particularly remarkable in view of the prematurity with its unstable heat regulating mechanism.

On the twelfth day of life, the baby vomited two of its feedings. The vomitus was streaked dark brownish. The next day the baby vomited three times, and some separation of the cranial sutures was noted. This finding was not considered unusual because premature babies frequently show signs of hydrocephalus. The same evening twitchings of the entire body were observed. On the fourteenth day the temperature rose to 106 F. There were marked convulsions and spasticity. These symptoms continued until the end. There was an occasional râle in the right axillary region. The vomitus was dark brown, but the Weber test for blood was negative. The infant was catheterized, and only a few drops of urine was obtained. There were many leukocytes, some of

which were in clumps, many granular casts, some of which were particularly large, and amorphous urates. No red cells were found. Subsequent urinalysis showed traces of albumin, reducing substance, acetone and granular casts, which diminished in number so that the last two specimens, on the twenty-first and thirty-second days, were free. Leukocytes persisted in the urine often clumped, and there were occasional red cells and epithelial cells. The cultures from the urine showed gram-negative bacilli and gram-positive cocci. There was no blood in the stool. A vaginal smear was negative; throat culture was negative; an eye smear taken from the discharge one day before death contained many leukocytes and a few cocci which were not morphologically gonococci.

The temperature tended to maintain itself between 99 and 102 F. for the rest of the time, although it was subnormal for the four days before death. On the twentieth day fine râles were heard in an area 4 cm. in diameter over the anterior surface of the left lung. They were heard at the end of deep inspiration after crying. Râles were also heard over the left upper lobe posteriorly. There were occasional râles over the right lung. The breath sounds were more distinct and sharper on the left side. Evidence of fine bronchitis persisted to the end.

On the twenty-fifth day two sharply demarcated, ulcerated areas appeared on the buttocks in symmetrical arrangement. That day the temperature was 104 F. The extremities were contracted and spastic. The diagnosis of meningeal hemorrhage was suggested. On the thirtieth day, in addition to the general spasticity, there was a sharp cephalic cry, and the anterior fontanel was bulging.

Spinal puncture yielded 4 c.c. of yellow fluid which appeared clear and in color resembled picric solution. A filmy pellicle separated out from the first tube in about five minutes. This tube contained the first 2 c.c. of fluid. There were 962 cells, most of which were polymorphonuclears. There were some red cells in the spinal fluid, but they were dissolved in acetic acid before the count was made. Therefore, some, at least, of these leukocytes came from the blood. Although massive coagulation did not occur, the expected large increase in globulins was proved by the Nonne, Ross Jones, Noguchi and Pandy tests, all of which gave heavy precipitates. Smears of the pellicle showed large numbers of polymorphonuclear leukocytes, considerable fibrin but no organisms by methylene blue, Gram or acid fast stains. The colloidal gold test showed reduction in the meningitic zone. The fluid was interpreted as indicating old blood in the cerebrospinal fluid. This would account for the yellow color, large quantities of globulin and cells. The predominance of white cells was accounted for on the theory that solution of red cells had occurred, leaving white cells and yellow color. The increase in polymorphonuclear cells would be explained on the increased polymorphonuclear content in the blood of the infant who also had a pyelitis and bronchopneumonia. This was probably the correct interpretation because the meningitis found on microscopic examination gave rise to round cell infiltration rather than polymorphonuclear cells.

On the thirty-first day, the spasticity of the extremities was still marked. On the thirty-second day the left lateral ventricle was punctured. Twenty c.c. of deep yellow fluid was obtained under greatly increased pressure. Following the puncture, the child became quiet, vomited and the bulging of the fontanel diminished. There were ninety-one cells, of which 78 per cent. were polymorphonuclears, 16 per cent. lymphocytes and 6 per cent. endothelial cells. There were also red cells, and the benzidin test was positive. The globulins were increased, although not to the same degree that they were found in the

spinal fluid. The ventricular fluid showed reducing substance. No bacteria were seen on smear, and in the cultures of both spinal and ventricular fluids there were no organisms. The Wassermann tests on both fluids were negative. The child died on the thirty-seventh day.

The necropsy was performed seven and one-half hours after death by Dr. Oscar Schultz. The fontanels were open and protuberant. When the dura was incised, considerable yellow fluid escaped. The inferior surface of the brain was yellow and was covered in areas by a layer of soft, pale yellow exudate between which the pia appeared congested and thickened. The lateral ventricles were distended and contained a slightly cloudy yellow fluid. The fluid

Fig. 1.—Lateral ventricles exposed, showing dilatation and exudate and enlarged choroid plexus. Exudate was pale yellow.

of the right lateral ventricle was darker than that of the left, but there was no brownish tinge. There were loosely adherent masses of opaque, yellowish white, soft material on the floor of the right ventricle. The right choroid was transformed into a soft red fleshy mass 2.5 cm. long and 0.6 cm. wide. The fourth ventricle was greatly distended. The dura of the cord was normal. The outer surfaces of the pia anteriorly had a yellowish tinge, and in the thoracic region the pia was thickened by a layer of grayish white material between pia and cord. Smears from the ventricular fluid and from the fibrinous material of the right ventricle contained no bacteria. In cultures from these sources a very small number of staphylococcus colonies developed.

Microscopic examination by George B. Hassin revealed a marked perivascular infiltration with lymphocytes and plasma cells, and marked vascular proliferation diffusely over the brain and cord. There were parenchymatous changes in the ganglion cells and proliferation of the glia. The markings between the gray and white substance were totally obliterated. There were areas of softening in the deeper layers of the white matter crowded with fat granular bodies. In one area a clump of bacilli was seen. The pia was

Fig. 2.—Fourth ventricle, showing dilatation.

markedly infiltrated with lymphocytes and plasma cells. There were numerous hemorrhagic foci. Throughout the specimen there were many microphages packed with hemoglobin and red cells. Careful microscopic examination ruled against the diagnosis of tuberculosis, although the original impression of a tuberculous lesion might have been made from a gross examination of the surface. He concluded that this was a case of meningo-encephalitis of some infectious origin and that the xanthochromia was undoubtedly due to numerous subpial hemorrhages.

The rest of the necropsy findings may be summarized briefly: The body was that of a poorly nourished white female 45 cm. long. There was very little subcutaneous fat. The serous cavities were normal. The foramen ovale was open to the extent of 2 mm. in diameter, otherwise the heart was normal. Both lungs were congested posteriorly, and the posterior portion of the right lung was firmer than the rest of the tissue. On section this was red, had a fleshy appearance and contained little air. The abdominal organs were apparently normal. Microscopic examination showed that the heart was negative. In sections from the posterior portions of the lungs, the bronchi were filled with polymorphonuclear cells, and in some of them the epithelium was desquamated. The septal vessels were distended, and the alveoli were filled with polymorphonuclear leukocytes. In one lung the consolidation was diffuse and widespread. In the other the areas of consolidation occurred about the bronchi,

Fig. 3.—Cord showing fibrinous deposit. This was yellow colored.

and air containing alveoli were present between the consolidated areas. In the anterior portions of the lung the septa were thicker than normal, due apparently to incomplete expansion. The lymphoid tissue of the spleen was small in amount. The tissue was greatly congested. The liver cells were moderately swollen. The pelvis of the kidney showed the subepithelial stroma diffusely infiltrated by lymphocytes, plasma cells and eosinophils. In one kidney the pelvic epithelium was absent in an area of considerable size, and the adjacent tissue of the medulla was diffusely and richly infiltrated with polymorphonuclear leukocytes. The cortex showed no involvement. The ureter and bladder were negative. The vessels of the suprarenal medulla were distended. The anatomic diagnosis, therefore, includes bilateral acute hypostatic pneumonia, bilateral subacute pyelitis and unilateral acute pyelonephritis.

We are not prepared to state the nature of the infection causing the meningo-encephalitis and subpial hemorrhages in our case, although the finding of a clump of bacilli in a necrotic area of the brain stimulates speculation. The only other case in the literature that corresponds to the findings of xanthochromia and red cells in the spinal and ventricular fluids present in our case is that of Horrax. This case, to which we have referred, occurred in a 12 year old boy from whom 40 c.c. of yellow spinal fluid was withdrawn which did not coagulate. It contained 1,011 old disintegrating red cells and eighty-five white cells. Fehling's solution was reduced; the Noguchi test was positive; and there were no tubercle bacilli. In our case the red cells were not counted, but there were 962 cells, most of which were polymorphonuclear. The ventricular fluid from Horrax's case, of which over 50 c.c. was withdrawn, contained 561 old red cells and seventeen lymphocytes. There was no massive coagulation, and Fehling's solution was reduced. We obtained 20 c.c. of fluid; the red cells were not counted. There were ninety-one white cells, 78 per cent. of which were polymorphonuclears, 16 per cent. lymphocytes and 6 per cent. endothelial cells. The benzidin test was positive, and reducing substance was present. The difference in cell findings is explained by the fact that the case of Horrax was one of pineal gland tumor while ours was a meningitis.

Other instances of ventricular puncture are noted but no xanthochromia. The cases of Leitch [14] and Hanes demonstrated that the ventricular fluid was clear while the spinal fluid was yellow, due to obstruction in the first case by tuberculous thickening and adhesions of the cervical membranes, and in the second to a tuberculous tumor blocking the pia-arachnoid at the level of the foramen magnum. The youngest case hitherto recorded was the case of Leitch, of tuberculous meningitis in a nine months old boy.

Our case belongs to the class of xanthochromic fluids without massive coagulation and with red cells. It might be termed a case of the incomplete xanthochromic syndrome containing red cells. This case may never have reached the complete stage. It is interesting to recall that Cestan and Ravaut stated in 1904, on the basis of their case of pachymeningomyletis of the conus that two factors may produce the syndrome of xanthochromia. coagulation *en masse* and increased cells. Although ours is not one of the complete syndrome, the factors

14. Leitch: Am. J. Dis. Child. **15**:348 (March) 1918.

stated by these authors are pertinent. One of the conditions they mention is a meningeal inflammation causing a serofibrinous exudate; the other is hemorrhage with solution of the red cells giving the yellow color to the fluid by freeing the hemoglobin. In our case both factors existed. This coexistence would tend to confirm Babinski's contention of a fibrinous hemorrhagic meningitis. However, this is only one of the conditions and not the most frequent, giving rise to yellow cerebrospinal fluid. Our case refutes the statement that in hemorrhagic meningitis the fluid is always red.

Therefore, we report the case of an infant living thirty-seven days of eight months gestation with xanthochromia of the cerebrospinal fluid due to a meningo-encephalitis, with numerous subpial hemorrhages as the source of the coloration.

DISCUSSION

DR. MILLER: In a case of meningococcus meningitis which I reported three years ago this condition was present. The child was 3 weeks old and the first lumbar puncture was negative and also the second. The third lumbar puncture failed to yield fluid; simply a gelatinous substance, of which only a drop adhered to the distal end of the needle. Finally, a ventricular puncture was made and the fluid obtained was yellow but it was not coagulated. I did not understand the condition at that time and I sent the specimen to Dr. Kolmer, who gave it the name xanthochromia. He remarked, as Dr. Abt has said, that such a fluid was due to the presence of a tumor or to chronic conditions causing continued compression of the spinal cord. I should like to ask Dr. Abt whether he found that the condition in his case was due to acute inflammatory process. Xanthochromia seems to be due to a constriction of the spinal canal, permitting a coagulation of the fluid. The fluid in my case was remarkably gelatinous. I should like to ask Dr. Abt also whether this condition occurs usually in young infants; my patient was young and I notice that he said his patient was 9 years old.

DR. ABT: The fluid was a deep yellow color, about the shade of picric acid. With relation to Dr. Miller's questions, in most of these cases the color is probably due to the dissolving of blood in the fluid. I have never seen a baby as young as the one reported with this condition; the literature shows few babies as young as this one. No organisms were found in the fluid though a very careful search was made. A specimen of the brain was sent to the pathologist who found a few bacilli which he was not able to identify.

REPORT ON AN EPIDEMIC OF HEMORRHAGIC DIARRHEA DUE TO STREPTOCOCCUS MUCOSUS

A. D. BLACKADER, M.A., M.D.

MONTREAL

April 14 I was summoned to Waterloo, a small manufacturing town on the Canadian Pacific Railway, about sixty miles southeast of Montreal, by Dr. Blake, one of its resident physicians, who told me that an epidemic of diarrhea had broken out suddenly in the town about three weeks previously. He had been called to see the first case March 22. Five additional cases developed on the following day, and since then new cases to a total number of sixty-five had been under his care in the town itself, and several more within a short radius of it.

The other physicians in the town were having a similar experience. Adults formed about one-fourth of the total number of the cases. Of the remainder, children under the age of 6 formed the largest number.

The illness began abruptly, as a rule, with high fever, nervous symptoms and anorexia. Vomiting at the outset was infrequent. Diarrhea set in early, with numerous stools of a greenish-brown color, of offensive odor, and containing much mucus and some blood. Both mucus and blood increased rapidly in amount as the movements became more frequent, and in the severer cases at the height of the disease appeared to form almost the whole of what was passed in the stools. There was, however, very little straining with the stool. Pain and symptoms of nervous irritation when present appeared chiefly before the movement took place, not after it. The same fact was noted in regard to vomiting, which when it did occur preceded defecation, or occurred during the act. Blood in the stools was a prominent feature in about 60 per cent. of the cases.

The attack lasted in some cases only a few days, but in the more severe cases the diarrhea and fever persisted for twelve, fourteen, or even twenty-one days. The number of the movements varied from five to thirty in the twenty-four hours. The temperature in a few rose as high as 106 F., but in the milder cases was comparatively low, from 100 to 102 F. In a few cases Dr. Blake did not observe any rise above

the normal. Notwithstanding the severity of the cases, only two deaths occurred in Dr. Blake's practice, but the subsequent exhaustion in many cases was extreme and persistent. He attributed the fatal ending in these two cases to cardiac weakness. One death took place suddenly after an attack of vomiting, associated with a movement of the bowels.

The report of an inspector sent out by the Provincial Board of Health at my request, stated that nearly one-half of the population of the town and district immediately surrounding it had suffered, but that the total mortality was only five.

REPORT OF CASES

CASE 1.—The patient whom I was called to see was a bright child of 6, who for the past five days had been suffering from a severe attack of this hemorrhagic diarrhea, with stools numbering from fifteen to twenty-six in the twenty-four hours. A sister, two years younger, had been one of the fatal cases referred to, and had succumbed suddenly after an illness lasting only six days.

I found my patient in bed in a well ventilated room, under the charge of a very intelligent mother and aunt. Her temperature at 8 p. m., taken in rectum just before my visit, was 103.4 F.; pulse, 140, weak but regular; respiration, 32. The skin was pale. The expression was one of exhaustion rather than pain. The child was mentally clear, complained of no pain, answered questions, and showed me her tongue, which was red tipped and moderately furred. There was complete anorexia, very little food had been taken for the past three days. During the day just passed nothing but water had been taken in small amounts about every half hour. There were no abnormal sounds in the lungs. Cardiac dullness was not increased. The abdomen was slightly distended and somewhat resisting. The spleen was not palpable, and splenic dullness did not appear to be increased, but was difficult to make out owing to the tympanic note over splenic flexure; the lower edge of the liver was palpable, a scant two finger-breadths below the costal margin. No special tenderness was made out in the right iliac region, but the condition present made one suspicious of a developing peritonitis. The stools which were shown to me contained an excess of mucus and some streaks of blood. The urine was scanty.

CASE 2.—A second child that I saw the same evening about 10 o'clock presented a different picture. The face was more pinched, the subcutaneous tissue very scanty, the abdomen shrunken and soft, the pulse weak and more rapid. The stool passed a few minutes before I entered the house was small in amount and contained considerable mucus and a small amount of unaltered blood. I did not see this child again. I am glad, however, to say that under careful nursing she recovered, but convalescence was very slow.

I saw the first child again at 5 a. m. the next morning before starting on an eight mile drive to catch a passing train on the main line. Her condition had not improved. The temperature and pulse were still high, but the abdomen had become more distended, the walls were more resisting, the movements of the diaphragm appeared limited.

In my opinion, there was no doubt of a peritonitis. Country roads in Spring were too rough to permit any thought of my taking her into the city, but I regarded her case as very grave. I gave the best hopes I could to the stricken mother, and over the telephone I kept in touch with the doctor. I am glad to say this child also slowly improved, and is now doing well.

An accident happened to the specimen of feces I brought back with me, but I had two fresh samples sent me by express. The report received from my bacteriologist, Dr. MacCordick, a former Fellow in Pathology under Dr. Adami, was as follows:

1. Direct smears show an intestinal bacterial flora consisting of (1) large numbers of chains of streptococci encapsulated; (2) about an equal number of bacilli coli; (3) very few of the other bacteria usually found in the stool; (4) no organisms of any type of bacillus dysenteriae.

2. Cultures on blood serum and agar show, macroscopically, a luxuriant greyish mucoid growth, smears from which show immense numbers of a streptococcus which after examination was regarded as a streptococcus mucosus.

3. The stool itself contains a large amount of mucus, some occult blood, and a small amount of undigested food.

The appearance of the specimen from the second child was somewhat different, a yellowish-brown watery stool, presented a well marked reaction chemically for mucus, but to the naked eye the amount of mucus appeared to be much less than in the previous specimen. The prevailing organism as in the former specimen was a streptococcus. These were very abundant and encapsulated. A large amount of pus was also present, much more than in the previous specimen. Reaction was neutral.

After culture on blood serum and on agar, there was a very abundant growth of the same organism as in the previous specimen. The amount of occult blood in this was distinctly less than in preceding specimens. The large amount of mucus present was regarded as due in measure to the mucus produced by the organism.

I regret that complete tests were not carried out in reference to its action on inulin, and its reaction to bile. I regret also that I had only these two samples examined, one sample from each child, but both Dr. MacCordick and myself were extremely pressed with work at the time, and I had hoped our provincial authorities would have carried out a very careful investigation. At my very urgent request a bacteriologist was sent out, but not till a fortnight after my visit, when the epidemic had ceased. His report on the dairy farms supplying the district with milk was that he could find no history nor any indication

of the presence of any infection of the udders, nor any disease in the cows supplying milk to the town, and the distribution of the cases did not appear to point to milk as the source of the infection. This had been the opinion also of Dr. Blake. The epidemic was not confined even at its outset to customers supplied by any one or even two milk dealers.

The epidemic arose suddenly, shortly after a few days of pronounced warm weather, when the snow melted rapidly on a still frozen soil. Waterloo has the reputation of having a good water supply. Nevertheless, in his report the health inspector stated that he found the water supply of the town to be derived from springs, several of which were at the time ineffectively protected against the surface drainage of adjoining property in which some cattle had been kept recently. As the result of his inspection he considered that contamination of the water supply had been the cause of the epidemic. The organism producing it was, in his opinion, a member of the typhoid group. Samples of blood taken from five adult patients who had suffered from the diarrhea gave a positive Widal reaction in four cases. This is opposed to my own view. The symptoms observed during the epidemic did not support his opinion, and the presence of an encapsulated organism in such large numbers, associated with the *Bacillus coli,* and the absence of any organisms of the bacillus dysenteriae type render it highly probable that this streptococcus was the true etiological factor in the production of this epidemic. Streptococci are well recognized as an important agent in the production of the deeper lesions of the intestine, but they appear, as a rule, to play the part of a secondary invader. Holt, however, states that the streptococcus is found at times in such overwhelming numbers that it is considered to play the chief part in the production of the symptoms.

I am unaware that any such epidemic as the one I have reported, due to this special form of streptococcus, has been observed before this one. I have found no note of such in literature.

DISCUSSION

DR. TALBOT: A few years ago, the summer following an epidemic of streptococcic sore throat, we had a large number of streptococcus diarrheas in the Floating Hospital. In these cases the predominating organisms were found in some instances in the blood and sometimes in the urine, and were associated in a large proportion of the cases with pyelitis. With the exception of that one summer we did not see anything similar in other years. I do not know the exact type of streptococcus isolated.

A STUDY OF PNEUMONIA IN INFANCY AND CHILDHOOD DURING RECENT EPIDEMICS *

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INTRODUCTION

During the past two years medical men have been confronted with the appalling spectacle of a most virulent epidemic that spread with terrifying rapidity over two hemispheres. The causative organism responsible for the influenza outbreak has not yet been definitely determined; but the high mortality was unquestionably due to the development of acute toxic pneumonias in a large proportion of the cases.

To the pediatrician, it seemed quite evident, early in the epidemic, that although infants and children were readily susceptible to the infection, the number that succumbed was comparatively small. Wollstein and Goldbloom,[1] however, in reporting a series of pneumonia cases in infants at the Babies' Hospital in New York City during a period of six weeks in the Fall of 1918, found a mortality of 57.7 per cent. (thirty out of fifty-two cases).

SCOPE OF PAPER

The following is an analysis of 336 cases of pneumonia admitted to the pediatric service at Mount Sinai Hospital during a period including the pandemic of 1918 and the recurrent wave of 1919. Not all of the cases were definitely influenzal in type. Most of them entered the hospital with a pneumonic process already developed, so that it was sometimes difficult to trace their origin. But the great proportion of the cases occurring during the epidemics were undoubtedly of this variety.

CLASSIFICATION OF CASES

Of 336 cases, 288 were bronchopneumonias, 48 lobar pneumonias; 56, or 16.6 per cent., succumbed. The cases of bronchopneumonia showed a mortality of 17.7 per cent. (51 our of 288 cases), and the age distribution was as follows:

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* From the Pediatric Service of the Mount Sinai Hospital.

1. Wollstein and Goldbloom, Am. J. Dis. Child. **17**:165 (March) 1919.

TABLE 1.—MORTALITY IN BRONCHOPNEUMONIA CASES

Age of Patient	Number of Cases	Number of Deaths	Percentage of Mortality
0 to 6 months	74	19	25.6
6 months to 1 year	70	14	20.
1 to 2 years	59	7	11.8
2 to 5 years	41	7	15.9
5 years	41	4	9.7

With the exception of the 2 to 5 year period, the mortality figures varied inversely with the age.

Of the forty-eight cases of lobar pneumonia 5, or 10.4 per cent., ended in death.

TABLE 2.—MORTALITY IN LOBAR PNEUMONIA CASES

Age of Patient	Number of Cases	Number of Deaths	Percentage of Mortality
0 to 6 months	0	0	0
6 months to 1 year	6	2	33.3
1 to 2 years	6	1	16.6
2 to 5 years	14	0	0
5 years	22	2	9

These figures compare very favorably with the statistics of pneumonia in infancy and childhood during previous years.

Pisek and Pease,[2] reporting 1,000 cases over a period of several years, found a mortality of 34.3 per cent.; Koplik[3] reviewed 1,351 cases admitted to the pediatric service of Mount Sinai Hospital between 1906-1914 and found a mortality of 18.3 per cent. In a report of the Babies Hospital,[4] September, 1914, of 51 patients with lobar pneumonia 5, or 10 per cent. died; of 116 cases of bronchopneumonia 62, or 33.1 per cent., ended in death.

PATHOLOGY AND BACTERIOLOGY

The left lower lobe was the most frequently involved in both lobar and bronchopneumonic cases. Holt,[5] in a report of 261 cases of bronchopneumonia, found the left lower lobe more extensively dis-

2. Pisek and Pease: Am. J. M. Sc. **151**:14 (Jan.) 1916.
3. Koplik, H.: J. A. M. A. **69**:1661 (Nov. 17) 1917.
4. Babies Hospital Twenty-Sixth Annual Report, Sept. 30, 1914.
5. Holt: Diseases of Infancy and Childhood, 1918.

eased than the right in more than two thirds of the cases. In our cases that came to necropsy, there were typical areas of consolidation in all stages, and hemorrhagic foci were a common finding.

Wollstein and Goldbloom,[1] from a study of the necropsy findings in eighteen cases in infants, report that the "characteristic features were purulent infiltrations of the alveolar walls and septa, hemorrhages and suppurative bronchiolitis."

A variety of organisms were found in the sputum in our cases, where obtainable. These included the influenza bacillus, pneumococcus, streptococcus and staphylococcus, but none in sufficient preponderance to justify any definite conclusions. In ten cases the sputum was examined for type pneumococcus and revealed: Type I, two cases; Type II, one case; Type III, none; Type IV, seven cases.

In twenty-four cases, specimens of blood were examined for type pneumococcus according to the method of Loewe, Hirschfeld and Wallach,[6] and showed: Type I, four cases; Type II, six cases; Type III, none; Type IV, fourteen cases.

The precipitin test in specimens of urine showed also Type IV most frequently present. Wollstein and Benson[7] found Type IV present in 60 per cent. of the cases reported in 1916.

One of our patients, showing Type I, received specific serum intravenously but succumbed from a severe toxemia.

ROENTGEN-RAY FINDINGS

Of twenty-eight roentgenograms of the chest taken in cases of lobar pneumonia, twenty-five showed definite shadows. Of seventy-three cases of bronchopneumonia, sixty showed more or less distinct shadows, which were interpreted as infiltrations. In eight cases in which no physical signs were elicited, but presented the clinical picture of pneumonia, the roentgen ray revealed the presence of lesions in the lung. We have found the roentgen ray of invaluable assistance in the diagnosis of both types of pneumonia.

BLOOD EXAMINATIONS

Of 200 blood counts recorded among our cases, the lowest leukocyte count was 4,000, with 40 per cent. polymorphonuclears. Another showed a count of 4,100 with 44 per cent. polymorphonuclears. Both patients died. We have found that a count below 10,000 and a polymorphonuclear count below 50 per cent. is significant of very poor

6. Loewe, Hirschfeld and Wallach: J. A. M. A. **73**:170 (July 19) 1919.
7. Wollstein and Benson: Am. J. Dis. Child. **12**:254 (Sept.) 1916.

resistance. The highest count was 86,000 with a polymorphonuclear count of 95 per cent. in a case with rapid recovery. The average blood picture was 25,000 leukocytes with 80 per cent. polymorphonuclears. Ten blood cultures taken in severe uncomplicated cases proved sterile.

COMPLICATIONS

The most frequent complication encountered was acute otitis media, which occurred in seventy-five of our 336 cases. Both ears were involved in forty cases. In general, our policy in treatment is a conservative one. Unless there is distinct bulging, we do not incise. In private practice, we find too many membranes opened without sufficient indications.

Empyema developed in seventeen cases. We advise strongly against early operation before the acute stage of the pneumonic process has subsided. The results obtained by watchful waiting in these cases are immeasurably better than immediate operative interference on the aspiration of pus from the pleural cavity. If dyspnea becomes marked due to the rapid accumulation of purulent fluid, potain aspiration is indicated.

In eight cases meningism, characterized by rigidity of the neck, convulsions, or spasms, delirium at times and a positive Kernig developed during the course of the pneumonia. In the severe cases lumbar punctures were done to relieve the increased cerebrospinal pressure.

In three cases lethargic encephalitis complicated the picture. Recent studies by Loewe and Strauss,[8] from the pathologic laboratory of Mount Sinai Hospital, throw new light on this condition. They believe it is a distinct disease produced by a specific organism which they have isolated in a large proportion of the cases.

In one case a hemiplegia and an embolus of the right external iliac artery developed necessitating amputation of the left lower extremity.

Two cases of severe acidosis with markedly decreased carbon dioxid tension proved fatal. There were two cases of spontaneous pneumothorax and one of diffuse subcutaneous emphysema.

One case was complicated by an acute suppurative pneumococcus meningitis. Blood culture as well as cerebrospinal fluid showed the

8. Loewe and Strauss: J. A. M. A. **73**:1056 (Oct. 4) 1919.

presence of Type I pneumococcus. Specific monovalent serum was injected intravenously and into the spinal canal, but without improvement. The patient succumbed about the tenth day.

One case was complicated by an acute purulent pericarditis. Blood culture was positive for Type I pneumococcus. Operation was performed, but the patient subsequently died of a continued general infection.

The rest of the complications included two cases of suppurative cervical adenitis, one of suppurative arthritis of the left shoulder, one of pyelitis in which bacillus coli was the invading organism, one gangrenous stomatitis, and one case of retropharyngeal abscess.

TREATMENT

Of prime importance in the treatment of pneumonia is the hygienic care and efficient nursing. Though much has been written about this aspect, it is still too often overlooked. A bright sunny room, with an abundance of fresh air, quiet surroundings and well trained nurses under close supervision are important essentials. A fretful, nervous mother should be excluded from the sick room. A modern hospital ward furnishes an ideal environment; but here, too, the greatest vigilance on the part of the physician must be exerted to guard against infections of the skin, eyes and mouth. A cleansing bath each morning should be a routine measure.

We do not favor the cold air treatment heralded several years ago with marked enthusiasm for any type of case. The gastro-intestinal tract should receive the closest attention. Milk diluted, gruels, fruit juices and an abundance of water form the chief elements of food.

Milk of magnesia in the morning and an enema each night are routine measures to insure proper elimination.

In the mild cases we have found the aromatic spirits of ammonia and liquor ammoniae anisatus useful for their mildly stimulating effect. They rarely produce any gastric disturbance. Whiskey in doses of from 10 to 20 drops, repeated every four hours, is of distinct advantage in producing temporary stimulation without the subsequent depression, which we have often seen following the administration of larger doses. Its caloric value too must be recognized.

For the moderately severe cases with high temperatures hydrotherapy, chiefly in the form of warm packs between 80 and 95 F., are

employed with good results. In addition, hypodermic injections of camphor and oil, and in some cases, where irritability is not marked, caffein and sodium benzoate are indicated.

For the very toxic cases these measures are used much more intensively, more frequent hypodermic stimulation and the warm packs applied at shorter intervals. Atropin and epinephrin are used in addition, with a view to prevent edema of the lungs.

We condemn the promiscuous use of dry cupping. We regard it merely as a demonstration of spectacular therapeutics and of no real value. The excitement and exertion for the patient attendant on its use certainly decreases his resistance.

We do not recommend the general use of digitalis. We have employed it in a considerable number of patients with no appreciable beneficial results. The pulse rate is not lowered, nor is the blood pressure raised. As auricular fibrillation is a very rare complication in the pneumonias of children, its use to prevent this condition is but an ephemeral theory.

In adults, encouraging results have been reported from the use of specific antipneumococcus sera. May we not look forward to further differentiation of types of organisms in the pneumonias of infants and children with the hope of securing specific therapy?

DISCUSSION

DR. PISEK: Dr. Heiman has brought out interesting facts about empyemas, and I would second what he has said about the need of patience, and giving the child a chance to fully develop the empyema before rushing him to the surgeon because he had a seropurulent exudate. The younger the child the greater the need of exercising patience. The surgeon is apt to be too enthusiastic in regard to the time of operation so I think we should stand between the patient and the surgeon and if necessary indicate the time when it is advisable to operate.

DR. GRIFFITH: It is interesting to notice the difference in different epidemics, not only in different years but in different localities. In 1918 and 1919 we saw in Philadelphia, in the influenza epidemic which struck us with unusual severity, a great deal of pneumonia; but everybody, I think, was impressed by the fact that the number of children suffering from it was small as compared with the number of adults, and that the disease in them was not nearly as severe. In the last epidemic of influenza in 1919 and 1920, which was much less severe, I was impressed by the large number of cases of pneumonia occurring in children, as well as by the large percentage which died. This was true both in the wards of the Children's Hospital, and in cases seen in consultation in private practice. Of course the hospital cases were naturally often very ill before they were brought to the institution, this being, indeed, the reason why they were brought. Still this was a reason which applied equally in other years when our mortality did not approach in the slightest degree

that seen in the past winter. There was a marked absence of leukocytosis in all of the cases of pneumonia, and the germ most often found was a hemolytic streptococcus. We noted, too, that it was extremely common to have empyema develop, and that this came on very insidiously. Empyema was, indeed, so often present that in cases which ordinarily we would have diagnosed as free from this, puncture was done as a precautionary measure, and repeatedly such cases would show fluid.

As to the time when operation should be done, this is perhaps a surgical matter, and yet the question is frequently put to us in the hospital by the surgeons whether the child is over its pneumonia. I am forced to say that it is a question which repeatedly we have been unable to answer. The cases in the past winter have not shown the usual drop of temperature with subsequent rise, but have developed empyema while the pneumonia was still present, and a continuance of fever made it almost impossible to tell when one process had ceased and the other begun.

DR. FREEMAN: I have enjoyed this excellent paper of Dr. Heiman's, but it seems to me his treatment is not good. I think we have no method of treating pneumonia so valuable as fresh air and the colder the air the better the patient does, the better his appetite is, the better he takes food, and the lower the temperature runs. I have never seen cold, fresh air do any harm in pneumonia and I have seen it do a great deal of good. In the use of fresh, cold air it is necessary to keep the extremities warm. The treatment of children with whiskey is not good. It may not harm older children. I have seen a great deal of whiskey used and believe it is injurious to babies. For many years I did not use digitalis, but recently I have been using it in large doses and it is very valuable, especially in older children when given early.

DR. BRENNEMANN: One point should be brought into relief in connection with this paper. Statistics based on hospital experience are so different from those in private practice that they do not represent the real degree of morbidity and mortality in pneumonia in children and I do not think that the statistics here given should go unchallenged. We know that in private practice there was no such high mortality even during the past two years as has been recorded in this paper. Then, too, the pneumonias that have occurred in the last two years have been wholly different from what we have been accustomed to and statistics based on them are not applicable in normal times. Even in epidemics such as those of the last two years the mortality varies very greatly in different epidemics and in different localities. My own experience in this respect is rather the opposite of Dr. Griffith's. In the October epidemic two years ago we saw very few pneumonias in children, but the mortality was frightfully high in those that had it. In the second epidemic I saw at least four times as many pneumonias with no mortality in private practice and a relatively lower mortality in hospital wards even though empyemas were unusually frequent.

Mortality statistics based on experience in hospital wards as in this paper are comparable to those usually given in our textbooks concerning the relative incidence of lobar and bronchopneumonia. Nearly all of these emphasize the much greater incidence of bronchopneumonia in infants and young children than of lobar pneumonia, whereas in general the exact opposite is true. These statistics are based on hospital experience, chiefly that of the Babies' Hospital, and largely on necropsy findings. As a matter of fact, we know that bronchopneumonia is peculiarly frequent only in infant hospitals and foundling homes. and also that nearly all babies that die of marasmus present the findings of a bronchopneumonia at necropsy. The same caution should be exercised in accepting the statistics that Dr. Heiman has given us.

DR. BLACKADER: I have listened with a great deal of pleasure to both the paper and the criticisms brought out in the discussion. I agree with the last speaker that hospital and private statistics represent two different phases; we at least find it so in Montreal. Unless the child is very ill and circumstances prevent proper nursing, mothers will not send their children to a hospital. The mortality given for lobar pneumonia is much higher than the average rate is in Montreal. I think alcohol may be used with advantage in some cases of pneumonia, but I do not think it is called for in every case. I heard one doctor say, "I am speaking as a pharmacologist, and I think alcohol should be given as a drug." I regard alcohol not so much as a drug but as a food, but it requires to be given in measured doses. Some children with pneumonia can take their nourishment without distress; in others digestion is much impaired, and the child does not get sufficient calories to support the heart. In alcohol we have a readily oxidizable agent, easily appropriated by the child, and one which may supply necessary nutrition for the heart and so do good.

As pediatrists we should not say use alcohol in pneumonia, but recommend its use only in such cases as cannot obtain sufficient nourishment in other foods. In such cases alcohol in measured doses, proportionate to the size and weight of the child, given at regular intervals, avoiding undue stimulation, may be used in pneumonia in children with advantage.

As to digitalis, it is apt to disturb the stomach; and any drug that upsets the stomach should be avoided. In children the cardiac muscle as a rule is fairly strong, and it is questionable whether death in pneumonia is due to failure of the heart muscle. In my opinion we should be careful in the use of digitalis.

I believe in fresh air, but I draw the line at fresh flowing air and strong draughts. Rest is very important. I hesitate about using a great deal of hydrotherapeutic treatment. The child may look forward to this with dread. If the child dreads the treatment, we may disturb and do more harm than we secure benefit. Complete rest, fresh air, and sufficient nutrition, with a minimum of abdominal distention, are all-important in the treatment of pneumonia.

DR. HOOBLER: Did you have many cases of unresolved pneumonia, in which you got the signs of pneumonia for two or three months, cases that you kept in the hospital, and the temperature came down but the signs of pneumonia remained? I have had a number of cases such as that. It was with a great deal of temerity that I would send these children home. I have found in such children that when they returned later the signs would have cleared up and they had not suffered at all from having been sent out with these unusual signs in the chest.

DR. SMITH: With reference to what has been said of the importance of quiet and rest, one of the most important things in the treatment of pneumonia is to conserve the outgo of energy. For this reason it is desirable to give morphin or codein in one form or another to lessen the cough.

DR. HEIMAN: It would be extremely difficult to give a formula for the treatment of pneumonia and in writing the paper that was not my intention. This paper is going to be read by the general practitioner and I have attempted to generalize. I know that the remedies suggested will not do much good but they will do no harm. Many of the carbolic acid group, creosote, guaiacol and a hundred others are used, and I do not know that they do a great deal of good. It is proper to wait until a pleural abscess is formed before opening the pleural cavity. If one waits until the abscess is walled in the results are very much better from the surgical standpoint. With reference to the high mortality in

hospital cases of which Dr. Griffith spoke, we all know that there are different strains of the organisms and that these children that come into the hospitals are often of low resistance, and as a consequence the mortality is high. When we are dealing with an empyema the roentgen ray is of considerable value if interpreted by a good interpreter, as it tells where the line of fluid is and whether one is dealing with ordinary solid lung or empyema.

With regard to the fresh air, I have found, as has been said, that it makes no difference whether you have a child in a hovel or on Fifth Avenue, whether you treat it with fresh air or with cold air, but I am in favor of fresh air for fresh air contains as much oxygen as cold air.

Dr. Blackader spoke of the fact that the results are better in private families. Of course in private families we get the cases earlier in the course of the disease than we do in the hospitals. In regard to alcohol, of course alcohol is a food. Every gram of alcohol contains seven calories. Alcohol promotes the circulation and anything that promotes the circulation promotes metabolism. In the application of hydrotherapeutics, I never use cold sponging, and I think when cold water is not used the fear can soon be overcome. Where the signs persist for a long time the structures all become involved and I think that explains some of the cases that present among the pathological findings multiple little hemorrhagic foci and a purulent exudate that requires a long time to resolve.

I am glad that Dr. Smith reminded us of the advantage of using codein; we use paregoric in infants and codein in older children. Potassium iodid, I think, does no good except in syphilis. I do not give pilocarpin because that salivates and I do not think that helps these children. I have often given syrup of hydriodic acid in small doses. Potassium iodid is bad as it upsets the stomach of a young baby.

FURTHER PROGRESS IN THE STUDY OF THE RELATIVE EFFICIENCY OF THE DIFFERENT MERCURIAL PREPARATIONS

IN THE TREATMENT OF CONGENITAL SYPHILIS IN INFANTS AND CHILDREN, AS DETERMINED BY A QUANTITATIVE ANALYSIS OF THE MERCURY ELIMINATION IN THE URINE *

WALTER R. RAMSEY AND O. A. GROEBNER

ST. PAUL

The treatment of syphilis with the different mercurial preparations is still a haphazard affair, the rule being to give as much mercury as the patient will tolerate without salivation or diarrhea.

Assuming that the amount of mercury eliminated in the urine during a given time would give a fair index of the amount in the circulation, Ramsey and Ziegler made some experiments, the report of which was read before this society in 1918.[1]

From this series of experiments we were able to draw the following conclusions:

In infants and children, mercury, when given by the month, by inunction or intramuscularly, is excreted at least partly by the urine.

In new-born infants and older children mercurial ointment when placed in contact with the skin, without any friction being used (protected and sealed by wax paper from being volatilized and inhaled), is taken up by the skin and excreted in the urine and continues to be excreted in the urine for a variable time after all treatment has been discontinued.

By inunction (with rubbing) mercury is readily taken up by the skin and eliminated in the urine and continues to be eliminated for a considerable time.

When one inunction is given, the maximum daily amount of mercury is usually eliminated during the following twenty-four hours, smaller amounts being eliminated for a variable time.

Where continuous inunctions are given, there is an accumulation in the system and considerable amounts are eliminated at intervals with only traces between.

Mercury salicylate suspended in oil and given subcutaneously continues to be eliminated in the urine in appreciable amounts for eight days, or longer, the daily amounts eliminated varying widely.

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* From the Department of Pediatrics, University of Minnesota.

1. Am. J. Dis. Child. **16**:299 (Nov.) 1918.

Mercuric chlorid by intramuscular method, a favorite method in congenital syphilis, continues to be eliminated for eight days or longer.

In all cases in which mercuric chlorid was used either by mouth or the intramuscular method, protein was found in the urine.

In this new series of experiments, we have sought to determine, with some degree of accuracy, the amount and rapidity of absorption of the common mercurial preparations in use as determined by quantitative estimate of the amounts eliminated in the urine.

The method is the same as that employed in the previous experiments.

TABLE 1.—UNGUENTUM HYDRARGYRI (50 PER CENT.) (1 GM. OF OINTMENT USED)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
M. S., 3½ years	Unguentum hydrargyri (50%) 1 Gm. as inunction	9/24	9/25	0.50	Congenital syphilis; Wassermann positive; female
			9/26	0.60	
			9/27	0.40	
			9/28	—	
			9/30	—	
	Unguentum hydrargyri (50%) 1 Gm. as inunction	10/ 1	10/ 1*	—	
			10/ 2	0.55	
			10/ 3	0.45	
			10/ 4	0.10	
			10/ 5	+	
			10/ 6	—	
			10/ 7	—	
	Unguentum hydrargyri (50%) 1 Gm. not by inunction	10/ 8	10/ 8*	—	
			10/ 9	0.40	
			10/10	0.20	
			10/11	0.12	
			10/12	+	
			10/13	—	
			10/14	—	
			10/15	—	
L. F., 5 years	Unguentum hydrargyri (50%) 1 Gm. as inunction	4/ 5	4/ 5*	—	Normal child; female
			4/ 6	+	
			4/ 7	0.42	
			4/ 8	0.12	
			4/ 9	+	
			4/10	±	
			4/11	—	
			4/12	—	
			4/13	—	
	Unguentum hydrargyri (50%) 1 Gm. not by inunction	4/14	4/14*	—	
			4/15	+	
			4/16	0.28	
			4/17	+	
			4/18	+	
			4/19	—	
			4/20	—	

* 24-hour specimen taken on day of administration of mercury.

It will be observed that when 50 per cent. ointment was used, the elimination began soon after administration, the maximum elimination occurring during the following three days, the elimination being fairly complete within five days.

TABLE 2.—Unguentum Hydrargyri (50 Per Cent.) (2 gm. of Ointment Used)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
D. H., 3 years	Unguentum hydrargyri (50%) 2 Gm. as inunction	7/31	7/31*	—	Congenital syphilis; Wassermann positive; female
			8/ 1	+	
			8/ 2	0.74	
			8/ 3	0.60	
			8/ 4	0.24	
			8/ 5	+	
			8/ 6	—	
	Same	8/ 7	8/ 7*	—	
			8/ 8	+	
			8/ 9	0.84	
			8/10	0.55	
			8/11	0.36	
			8/12	+	
			8/13	+	
			8/14	—	
			8/15	—	
	Unguentum hydrargyri (50%) 2 Gm. not as inunction	8/16	8/16*	—	
			8/17	+	
			8/18	0.34	
			8/19	0.14	
			8/20	+	
			8/21	—	
			8/22	—	
			8/23	—	

* 24-hour specimen taken on day of administration of mercury.

TABLE 3.—Unguentum Hydrargyri Dilutum (33 Per Cent.)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
M. S., 3½ years	Unguentum hydrargyri dilution (33%) 2 Gm. as inunction	10/15	10/15*	—	Congenital syphilis; Wassermann positive; female
			10/16	0.20	
			10/17	+	
			10/18	+	
			10/19	—	
			10/20	+	
			10/21	—	
	Unguentum hygrargyri dilution (33%) 2 Gm. as inunction	10/22	10/22*	—	
			10/23	+	
			10/24	+	
			10/25	—	
			10/26	+	
			10/27	—	
			10/28	—	
			10/29	—	
A. E., 7 years	Unguentum hydrargyri dilution (33%) 2 Gm. as inunction	4/ 5	4/ 5*	—	Normal child; male
			4/ 6	0.10	
			4/ 7	+	
			4/ 8	+	
			4/ 9	+	
			4/10	+	
			4/11	—	
			4/12	—	
	Unguentum hydrargyri dilution (33%) 2 Gm. not as inunction	4/13	4/13*	—	
			4/14	+	
			4/15	+	
			4/16	—	
			4/17	—	
			4/18	+	
			4/19	—	
			4/20	—	
			4/21	—	

* 24-hour specimen taken on day of administration of mercury.

When double the amount, 2 gm. of the 50 per cent. ointment, was used as inunction, the amounts eliminated were relatively larger.

With the 33⅓ per cent. mercurial ointment, even when double the quantity was used, the elimination did not begin in appreciable amounts until the second day after inunction, and then in much less quantities than when the 50 per cent. ointment was given.

TABLE 4.—CALOMEL UNGT. (30 PER CENT.)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
L. F., 5 years	30% calomel unguentum 2 Gm. as inunction	4/20	4/20*	—	Normal child; female
			4/21	—	
			4/22	+	
			4/23	0.12	
			4/24	+	
			4/25	—	
	Same as above	4/26	4/26*	—	
			4/27	—	
			4/28	+	
			4/29	0.24	
			4/30	+	
			5/ 1	—	
			5/ 2	—	
			5/ 3	—	
J. B,. 3 years	30% calomel unguentum 2 Gm. as inunction	8/15	8/15*	—	Congenital syphilis; Wassermann positive; female
			8/16	—	
			8/17	+	
			8/18	0.14	
			8/19	+	
			8/20	—	
			8/21	—	
			8/22	—	
	Same as above	8/23	8/23*	—	
			8/24	—	
			8/25	+	
			8/26	0.30	
			8/27	+	
			8/28	—	
			8/29	+	
			8/30	—	
	30% calomel unguentum 2 Gm. not as inunction	8/31	8/31*	—	
			9/ 1	+	
			9/ 2	+	
			9/ 3	—	
			9/ 4	+	
			9/ 5	—	
			9/ 6	—	
			9/ 7	—	
	30% calomel unguentum 2 Gm. not as inunction	9/ 8	9/ 8*	—	
			9/ 9	+	
			9/10	—	
			9/11	+	
			9/12	+	
			9/13	—	
			9/14	—	
			9/15	—	

* 24-hour specimen taken on day of administration of mercury.

When the mercurial ointment was simply used by smearing on the skin, without rubbing, the amount eliminated was much less than when used as an inunction.

In the case of calomel ointment, it will be seen that the elimination is delayed, and the total quantity eliminated is much less than with the mercurial ointment, although two grams were used for each inunction.

With the mercurial salicylate in oil, used hypodermically, it will be seen that the maximum elimination is in the first twenty-four hours—smaller quantities continuing to be eliminated for six or seven days.

TABLE 5.—MERCURY SALICYLATE IN OIL (INTRAMUSCULAR INJECTION)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
J. F., 3½ years	Mercury salicylate (0.065 Gm.) in oil; intramuscular injection	4/ 5	4/ 5*	—	Normal child; male
			4/ 6	0.65	
			4/ 7	0.16	
			4/ 8	+	
			4/ 9	+	
			4/10	+	
			4/11	+	
			4/12	—	
			4/13	—	
	Same as above	4/14	4/14*	—	
			4/15	0.55	
			4/16	+	
			4/17	+	
			4/18	+	
			4/19	+	
			4/20	—	
			4/21	—	
M. L., 4½ years	Same as above	4/20	4/20*	—	Normal child; female
			4/21	0.46	
			4/22	+	
			3/23	+	
			4/24	+	
			4/25	+	
			4/26	—	
			4/27	+	
			4/28	—	
			4/29	—	
M. B., 6 years	Same as above	8/15	8/15*	—	Congenital syphilis; female
			8/16	0.60	
			8/17	0.18	
			8/18	+	
			8/19	+	
			8/20	+	
			8/21	+	
			8/22	+	
			8/23	—	
			8/24	—	

* 24-hour specimen taken on day of administration of mercury.

The mercuric chlorid solutions used hypodermically continued to be eliminated in amounts not sufficient to be measured for six or seven days. In one case there was an appreciable amount of protein in the urine following its use, a point which we also observed in our previous experiments.

TABLE 6.—MERCURIC CHLORID (INTRAMUSCULAR INJECTION)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
M. L., 4½ years	Mercuric bichlorid, 0.5 C.c. of 10% solution intramuscularly, i. e. 0.005 Gm. of mercury	4/ 5	4/ 5*	—	Normal child; female
			4/ 6	++	
			4/ 7	+	
			4/ 8	+	
			4/ 9	+	
			4/10	+	
			4/11	—	
			4/12	—	
			4/13	—	
	Same as above	4/14	4/14*	—	
			4/15	++	4/15, urine gave faint protein test
			4/16	+	
			4/17	+	
			4/18	+	
			4/19	—	
			4/20	—	
J. F., 3½ years	Mercuric bichlorid, 0.5 C.c. of 1% solution intramuscularly, i. e. 0.005 Gm. of mercury	4/20	4/20*	—	Normal child; male
			4/21	++	
			4/22	+	
			4/23	+	
			4/24	+	
			4/25	+	
			4/26	+	
			4/27	—	
			4/28	—	

* 24-hour specimen taken on day of administration of mercury.

TABLE 7.—CALOMEL (BY MOUTH)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
M. F., 7 years	Calomel 1 grain by mouth	4/ 5	4/ 5*	—	Normal child; female
			4/ 6	+	
			4/ 7	+	
			4/ 8	+	
			4/ 9	+	
			4/10	+	
			4/11	—	
			4/12	—	
			4/13	—	
	Calomel 1 grain by mouth	4/14	4/14*	—	
			4/15	+	
			4/16	+	
			4/17	+	
			4/18	+	
			4/19	+	
			4/20	—	
M. B.,	Calomel ¼ grain by mouth every 4 hours for 4 doses	8/24	8/24*	—	Congenital syphilis; female
			8/25	+	
			8/26	+	
			8/27	+	
			8/28	+	
			8/29	+	
			8/36	+	

* 24-hour specimen taken on day of administration of mercury.

Calomel given by mouth (1 grain) either in one dose or divided doses, was eliminated in appreciable amounts although not sufficient to be measured for six or seven days.

Gray powder, although given in large doses, was eliminated to a very small extent and for a short period of time.

The practical deductions which may be drawn from this series of experiments are, therefore, as follows:

TABLE 8.—GRAY POWDER (BY MOUTH)

Name and Age	Amount and Method of Administration of Mercury	Date of Administration	Date of 24-Hour Specimen	Amount of Mercury in Mg.	Remarks
M. F., 7 years	Gray powder 3 grains by mouth every 4 hrs. for 4 doses	4/20	4/20*	—	Normal child; female
			4/21	±	
			4/22	+	
			4/23	+	
			4/24	—	
	Same as above	4/25	4/25*	—	
			4/26	+	
			4/27	—	4/26 Frequent stools; some tenesmus
			4/28	+	
			4/29	+	
			4/30	—	
			5/ 1	—	
M. S., 3½ years	Gray powder 3 grains by mouth	11/24	11/24*	—	Congenital syphilis; female
			11/25	±	
			11/26	—	
			11/27	—	
			11/28	—	
	Gray powder 3 grains once daily for 5 days	11/29	11/29*	—	
		11/30	11/30*	—	
		12/ 1	12/ 1*	+	
		12/ 2	12/ 2*	±	
		12/ 3	12/ 3*	±	
			12/ 4	+	
			12/ 5	—	
	Gray powder 3 grains every 4 hours for 4 doses	12/ 6	12/ 6*	—	
			12/ 7	—	
			12/ 8	0.14	
			12/ 9	+	
			12/10	—	
			12/11	—	
			12/12	—	
			12/13	—	
			12/14	—	

* 24-hour specimen taken on day of administration of mercury.

1. Mercurial ointment, 50 per cent., is to be preferred to the less concentrated forms and need not be repeated more often than twice weekly instead of daily. The quantity of mercury absorbed is much increased by friction.

2. Calomel ointment is absorbed but less rapidly and to a less extent than the mercurial ointment and should, therefore, be given in greater concentration.

3. The salicylate of mercury in oil should be given hypodermically twice weekly instead of once.

4. The mercuric chlorid, by hypodermic injections, although the dose is very small, continues to be eliminated for six or seven days. The fact, however, that its use frequently is followed by the appearance of protein in the urine should exclude it from the treatment of syphilis in children.

5. Calomel by the mouth is absorbed in small amounts, and continues to be eliminated for a considerable time so that it is probable that it would be sufficient to give it at intervals of several days, thus avoiding diarrhea.

6. Gray powder is absorbed to a small degree and eliminated rather rapidly so that large doses repeated daily would probably be necessary to maintain mercury in the circulation.

We shall continue our experiments and determine, if possible, whether the clinical results will bear out the observations made in these experiments. In one case (M. S.) of congenital syphilis, with marked keratitis, treated by inunctions of 50 per cent. mercurial ointment, once weekly, the clinical progress was apparently quite as satisfactory as in cases where daily inunctions were given.

DISCUSSION

DR. DEBUYS: In looking over the charts I see M. S. in the first and D. H. in the second, and in neither case was there a second administration of the drug and there is a greater elimination of mercury than in other cases. These apparently are the only two cases of the kind in this study. I would like to ask Dr. Ramsey if he has studied the elimination in his cases with the daily administration of the same drug.

DR. GERSTENBERGER: Have you given gray powder in 0.5 gm. doses, three or four times a day? This can be administered without causing diarrhea and the results are very satisfactory from a clinical standpoint. I wonder if you have checked up the excretion on such small doses.

DR. FLEISCHNER: Have you made any estimation of the amount and duration of mercury in the stools of these children?

DR. RAMSEY: If you will read the report on the work published in the *American Journal of Diseases of Children*, November, 1918, you will see that we made a similar analysis of cases in which the drug was given continuously. One would find a great deal of mercury one time, then a very little or none and then a great deal again. In some of the children it was very difficult to get complete twenty-four hour specimens; we had to do what we could

with the few cases in which we could get complete specimens. We had the greatest difficulty in the young infant in which we could get very few twenty-four hour specimens which we could depend on.

As to why I did not give opium. That is a clinical question and we were just observing what happened ordinarily as regards elimination.

We did not make any examination of the stools. We aimed to know the amount in the circulation and that we could know by finding the amount eliminated in the urine, but the amount in the feces would not have told us anything about the absorption.

A STUDY OF THE INCIDENCE OF HEREDITARY SYPHILIS*

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Several estimates have been made of the incidence of hereditary syphilis, but none has been based on observation that renders it applicable to the community at large. Studies on hospital and dispensary cases give the incidence only in the poorer class or more particularly in the sick of this class. All estimates based on older children do not take into account the stillborn infants and those dead in early infancy, many of which deaths are due to hereditary syphilis. Such estimates are thus somewhat misleading. Few attempts have been made to secure figures applicable to the middle and upper social classes. A true estimate of the incidence of hereditary syphilis, therefore, should be based on observations which included all children born in a group of unselected families of all classes.

In the present study the method used was the histologic examination of a series of placentas, together with a Wassermann reaction on the fetal blood collected from the umbilical cord at birth. In order to determine the reliability of such a method, it was necessary to secure additional Wassermann reactions on the mother, and on the infant after two months in as many cases as possible. It has been shown that there is a high percentage of agreement between the result of the Wassermann reaction on the maternal blood and histologic evidence of syphilis in the placenta. The necropsy findings in stillborn infants likewise correspond closely with the placental histology in so far as syphilis is concerned. We hoped, therefore, that a similar close agreement could be demonstrated between the placental histology and fetal blood Wassermann, on the one hand, and the living infant, on the other, in which case the incidence of hereditary syphilis in the middle and upper classes could be estimated by examination of the placenta and cord blood.

* From the Department of Pediatrics, Washington University. Aided by a grant from the United States Interdepartmental Social Hygiene Board.

One point about the histologic study of the placenta may be mentioned. It is not certain that the same pregnancy can produce a syphilitic child and a placenta free from syphilitic changes, although it is rare to find any organ universally affected by this disease. It seems quite likely that the changes of syphilis in the placenta are not always diffuse, and that if one could make an extensive search, areas showing characteristic changes might be found in all cases in which the infant is syphilitic. This question is of little practical importance, however, since it is impossible to make routine serial sections and in such a study as the present one, only a diffuse placental change can be considered, although in doubtful cases we have examined sections from several areas.

Our material was collected from several constant sources and included about one fifth of the children born in St. Louis over a period of months, almost equally divided between charity and private patients. In the former group only was it possible to secure additional blood examinations of mother and infant in a number of instances after two months. The study is being continued and the results herewith presented are based on the data thus far collected from the first 1,000 cases.

Up to the present time we have been able to examine 129 infants, 2 or more months of age. Of these 10 per cent. presented undoubted evidence of syphilis and the remainder were just as evidently non-syphilitic. The evidence of infection consisted chiefly of a strongly positive Wassermann reaction. Classification of this group according to race shows an incidence of 15.8 per cent. among the negroes and 5.5 per cent. among the whites.

The chief point of interest in this group, however, is the relation of the established diagnosis in the infant to the histology of the placenta and to the Wassermann reaction on the placental cord blood. The histologic diagnosis on the placenta as to the presence or absence of syphilitic changes corresponded to the established diagnosis of the infant in 95.5 per cent. of the cases. The lack of correspondence consisted entirely in finding no syphilitic change in the placenta in cases in which the infant had syphilis. In every instance in which the placenta was noted as showing syphilitic changes the infant was later found to have syphilis. Considering the syphilitic cases alone, the microscopic examination of the placenta failed to show evidence of syphilis in 50 per cent.

In this same group of infants in which the diagnosis was established. the Wassermann reaction on the placental cord blood corresponded to the diagnosis in the infant in 96.5 per cent. Here, also, the discrepancies were entirely due to the finding of a negative Wassermann reaction on the fetal blood in instances in which the infant was syphilitic. In every instance in which the fetal blood gave a positive Wassermann reaction the infant was later found to have syphilis. On the other hand, when the infant was later shown to be syphilitic the cord blood Wassermann was found to have given evidence of that fact in only 57 per cent. of the cases.

Of the 1,000 cases considered in this report, 574 patients were of the dispensary or poorer class. On the basis that the number of positive placentas is one half the total number of cases of infantile syphilis, we find that in the infants of this group there was an estimated incidence of syphilis of 9.6 per cent. Classified according to race the incidence among the negroes was found to be 14.4 per cent. and among the whites 5.8 per cent.

On the basis that syphilitic infants give a positive Wassermann reaction on their cord blood in only 57 per cent. of cases, we find that the estimated incidence of infantile syphilis in the 574 pregnancies among the poorer class is 10.5 per cent.

It is observed that the incidence in the group of 574 patients as estimated from the placental examination (9.6 per cent.) corresponds very closely to that estimated from the Wassermann reaction on the cord blood (10.5 per cent.). It is also observed that the incidence *estimated* by these two methods (9.6 per cent. and 10.5 per cent.) on a large number of infants corresponds closely to the *established* incidence (10.5 per cent.) in a smaller group of the same social class. This fact tends to confirm the reliability of the methods of estimation and establishes the justification for applying either or both methods of estimation among other social classes.

Of the 1,000 cases of this report 426 were classed as private patients. These patients were able to pay a physician's fee and private room rates in a hospital, and, therefore, belong to the middle and upper social classes. Examination of the placentas of this group showed three positive placentas and one which was classed as doubtful. Excluding the doubtful case the estimated incidence was 1.4 per cent. Including the doubtful case the estimated incidence was 1.9 per cent. Estimating the incidence in the same manner from the Wassermann reaction on the

cord blood there was found an incidence of 1.6 per cent. Thus there is very close agreement between the incidence estimated from the placental examination and that estimated from the Wassermann reaction on the cord blood. It was, perhaps, a coincidence that the positive cord bloods and the positive placentas in this group were not observed in the same cases, which fact gives additional justification for doubling the number found by either method alone in the estimation of the incidence of syphilis.

Though the chief aim of this study was to determine the general incidence of hereditary syphilis several other features of interest have developed. Some of these may be briefly enumerated. The maternal Wassermann was obtained in 163 instances. In this group an agreement of 91 per cent. was found between the result of the maternal Wassermann reaction and the histologic examination of the placenta. In two instances of disagreement the mother had syphilis but was treated during the later months of pregnancy, resulting in the birth of a nonsyphilitic infant. In two instances the mother gave a negative Wassermann reaction and yet each gave birth to a syphilitic infant, both the placentas showing positive changes. In most instances in which the maternal Wassermann reaction was positive and the placenta negative the infant was shown to be syphilitic. On three occasions the mother had a positive Wassermann reaction but without specific treatment gave birth to a nonsyphilitic infant. In one of these the mother's Wassermann reaction was only weakly positive. Leaving out of consideration the cases influenced by treatment the agreement of the maternal Wassermann reaction with the diagnosis of the infants was 95 per cent.

In some instances in which the infant had syphilis the maternal Wassermann reaction alone was positive, in others the placenta alone was positive. Therefore, in order to give a clean bill of health to an infant at birth it is necessary to have all three examinations negative (maternal Wassermann reaction, placenta, cord blood) and even then there may be some uncertainty.

The fact that treatment of the mother during pregnancy or even during the later months of pregnancy will result in the birth of a nonsyphilitic child has been established by previous observations. In this series are two instances in which the mother received treatment during the later months, resulting in the birth of a nonsyphilitic infant even

though the mother's Wassermann reaction was still positive. In two other instances the mother had treatment sufficient to cause a negative Wassermann reaction and gave birth to a nonsyphilitic infant.

We hope that in the further analysis of a larger series of cases, the increased number of examinations will render the estimate more convincing. From the present study, however, we have made the following inferences:

There is an incidence of hereditary syphilis of 5.5 per cent. among the poor of the white races, 16 per cent. among the negroes and 10 per cent. for the whole group of the dispensary class. The incidence among the combined middle and upper social classes is in the neighborhood of 1.5 per cent. The total incidence in the entire group of 1,000 cases is 6 per cent. It is our feeling that the entire group fairly represents a cross section of the population of St. Louis and if such is the case the incidence of hereditary syphilis in St. Louis at the time of birth is 6 per cent. When syphilitic changes are present in the placenta, the infant has syphilis even though the Wassermann reaction is negative on the fetal blood, and, vice versa, the infant has syphilis if the cord blood shows a positive Wassermann even though the placenta appears normal. The infant may be syphilitic if both placenta and cord blood are negative. A syphilitic child may be born to a woman with a negative Wassermann, and a mother with untreated syphilis and strongly positive Wassermann reaction may have a healthy child.

DISCUSSION

DR. GERSTENBERGER: I have a statement made by Dr. Burhaus who went over the records of the Babies' Dispensary during the last year for cases of congenital syphilis among the 20,000 patients we have had since 1906. He found a very low percentage diagnosed on the basis of clinical observation. During the last six years we have checked up with the Wassermann reaction and we found very little increase over what we found before using it, a total for both periods of a little over 1 per cent. I am sure we must be wrong, but I want to report just what we found. Among the negroes 14 per cent. were syphilitic and the highest number of syphilitics occurred among the poor whites of American ancestry, 27 per cent. The highest number occurred among the poor whites, next came the negroes, then the Italians, and the least were found among the Jews.

One woman came with twins, 8 weeks old, one of whom showed unmistakable skin symptoms of syphilis while the other was perfectly normal. The Wassermann corresponded with the clinical picture. Both are alive today. The child that had the negative reaction at birth still has a negative reaction, while the brother with the positive reaction was treated with mercury and improved,

but he still has a positive reaction. How are we going to interpret this finding? In all probability there was a break in that part of the placenta with which this child with the positive Wassermann had his connection.

DR. BRENNEMANN: Did you check up all cases or only those supposed from clinical signs to have syphilis.

DR. JEANS: Only those that were suspicious, those that clinically gave evidence of syphilis.

DR. HEIMAN: Have you had any experience with cases of congenital lues subjected to treatment and then a second Wassermann test made. Some have reported that in congenital lues once a Wassermann positive always a Wassermann positive. I should be glad to hear whether Dr. Jeans has made any such studies on congenital lues.

DR. DEBUYS: I wish to emphasize the necessity of making a Wassermann test on each individual infant irrespective of what the mother's reaction may be. We have seen mothers negative from the Wassermann standpoint and in apparently perfect health and yet their children were decidedly luetic as was shown by positive Wassermann tests. We have had instances such as the one cited by Dr. Gerstenberger in which the mother and one twin have both given positive Wassermann reactions while the other twin with a negative Wassermann was apparently healthy.

DR. JEANS: Any statistics based on clinical examination alone are found to give a lower incidence of syphilis than those based on the Wassermann reaction. We have no statistics which include the older children, but among these one would get a lower incidence because there is a high infant mortality due to hereditary syphilis. We have tried to eliminate both of these factors and to get at the truth by taking both the cord blood and the placenta at the time of birth.

Dr. Heiman asked whether there could be a serologic cure in hereditary syphilis, and whether that would be true of infants and not of older children. We have been getting a negative serologic result in every instance in which the child came for the required time and was treated, so that I would say it was not only possible to get a negative serologic result in congenital syphilis, but that it was the rule under proper treatment.

With regard to twins, sometimes only one will give a positive reaction and sometimes both will be positive. The reports are about equally divided as to one or both giving positive reactions, with perhaps a slight preponderance in favor of both infants being infected.

As to the placental blood becoming anticomplementary, very few were so found, so few that we did not think it worth while to report the incidence of that finding.

PRELIMINARY OBSERVATIONS ON THE PATHOGENICITY FOR MONKEYS OF THE BACILLUS ABORTUS BOVINUS*

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The importance of accurate determinations as to the pathogenicity of the *B. abortus bovinus* can hardly be overestimated, when one realizes that infectious abortion of cattle is present in practically all herds, and that the organism is invariably found from time to time in the milk of all infected animals.

In 1894, Theobald Smith called attention to a peculiar disease resembling tuberculosis occurring in guinea-pigs, following the inoculation of milk. It was not until 1911, however, that he, with Marshal Fabyan as a co-worker, determined that these lesions were due to the *B. abortus bovinus,* and emphasized the desirability of discovering the possible rôle that this organism might play in human pathology. Since then the great prevalence of *B. abortus* in raw milk has been proven by numerous investigators, notably Schroeder. and Cotton in this country and Zwick and Krage in Europe.

In 1916, Alice C. Evans published a most comprehensive piece of work on the bacteria of milk, using a special method of plating, whereby she determined that the *B. abortus* was present in about 25 per cent. of all samples studied. In 1915 and 1916, in an effort to learn the incidence of tubercle bacilli in certified milk, we injected the sediment of large quantities of milk into guinea-pigs, and found that inoculation experiments demonstrated the constant presence of *B. abortus* in the certified milk produced in the environs of San Francisco. Evans, in 1918, in a most illuminating piece of work, showed that the *B. abortus* and the *B. melitensis* were morphologically, serologically and biochemically practically indistinguishable. In 1919, following the injection of guinea-pigs with these organisms, we were able not only to confirm Evans' findings, but to prove that animals with abortion disease showed positive cutaneous hypersensitiveness,

* From the George Williams Hooper Foundation for Medical Research and the Department of Pediatrics of the University of California Medical School.

using either abortin or melitensin as an antigen, and, vice versa, those guinea-pigs with *B. melitensis* lesions gave equally strong skin tests, whether the abortin or melitensin was used. If one grants the usually accepted opinion as to the specificity in guinea-pigs of cutaneous hypersensitiveness, the close relationship of these organisms becomes more apparent.

Only by a series of absorption tests was it possible to differentiate the type of infection. The *B. melitensis* is the recognized cause of undulant fever in man. The disease occurs primarily in goats through whose milk human infection takes place with great ease. It is a striking fact that the clinical picture produced by the *B. melitensis* in goats is similar to that produced by the *B. abortus* in cattle, namely, infectious abortion, although both sets of animals may harbor their respective organisms, and having acquired a great degree of immunity, show few symptoms.

Even more striking than this, however, was the fact that in several sets of guinea-pigs, following the intratesticular injection of *B. melitensis,* the lesions, macroscopic and microscopic, occurring in the spleen and lymph nodes were indistinguishable from those produced by *B. abortus.*

In endeavoring to determine the pathogenicity of an organism for man, positive results in the lower laboratory animals are of little practical value. It becomes necessary, therefore, to gather data by endeavoring to infect monkeys. The literature records considerable work that has been done in infecting monkeys with *B. melitensis.* Not only by the subcutaneous and intravenous injection of the organism is it possible to get a definite infection, but by feeding a single sample of infected milk, the animals run characteristic temperatures and develop a disease which is very similar to that seen in man. Careful review of the work that has been done with the *B. abortus,* however, shows that only one investigator used monkeys in an effort to produce a characteristic disease. Marshal Fabyan infected two monkeys and was able to recover the organism twelve and thirteen weeks, respectively, after the inoculation. He does not state the method used in inoculating the animals and gives no additional observations as to the results.

In an effort to determine the pathogenicity of the *B. abortus bovinus* for monkeys, the following experiments were carried out:

RECORD OF EXPERIMENTS

MONKEY 1.—Feeding Experiment. April 3, 1919, fed 2 slants of *B. abortus* 152. Agglutination reactions April 9 and 21, and July 8 were negative. Died of intercurrent disease. Necropsy negative. Cultures negative.

MONKEY 2.—Intravenous Inoculation. April 3, 1919, injected one-fifth slant of *B. abortus* 80 (age of culture, 2½ years) into the left jugular vein. Good response by agglutinin production. May 24, chloroformed. Length of experiment fifty-one days. *B. abortus* isolated from the right and left kidney, spleen and liver. Agglutination tests: Abortus 80, 1:4,000+ and 1:1,000+++. *B. melitensis* 1, 2, 3, 4 and 5, 1:600+++, 1:1,000+ (Fig. 1).

MONKEY 3.—Feeding Experiment. Fed daily from July 2 to Aug. 24, 1919, between 150 and 50 c.c. of the milk of an infected goat.* From August 24 to Sept. 30, 1919, fed the same milk irregularly, depending on its production.

From October 4, to November 10, the monkey was fed daily one slant of *B. abortus* 80 and one slant of *B. abortus* 14 (age of culture, 10 years) on bread. He died November 12, of bronchopneumonia. (Duration of experiment, 133 days.)

B. abortus was recovered from the spleen. Serum of animal agglutinated *B. abortus* 80 in dilution of 1:600+++ and *B. abortus* 14 in dilution of 1:200+++.

MONKEY 11.—Intravenous Inoculation. Aug. 6, 1919, injected one-quarter slant *B. abortus* 14 intravenously. Agglutination reactions August 21, fifteen days after inoculation, *B. abortus* 80 1:2,000+++, *B. melitensis* 1:800++ and *B. melitensis* 1:600+++. Died November 12, of intercurrent disease. (Duration of experiment ninety-eight days.) Necropsy negative. Cultures contaminated. Agglutination reactions *B. abortus* 80, 1:40. *B. melitensis* all negative.

MONKEY 12.—Intravenous Inoculation. Aug. 14, 1919, injected intravenously one-quarter slant *B. abortus* 80. Monkey passage No. 2. August 18, animal died. (Duration of experiment four days.) *B. abortus* recovered from all of the organs; liver, spleen, lymph nodes, kidneys and bone marrow. Heart's blood sterile.

MONKEY 19.—Feeding Experiment. From Sept. 30, to Oct. 30, 1919, was fed goat's milk which was very rich in agglutinins, but very poor in organisms. Agglutination tests with the serum of this monkey were all negative. Died

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* The history of the goat whose milk was used in this feeding experiment is as follows:

GOAT 1.—Infected June 2, 1919, by an injection of *B. abortus* 80 into the right udder. June 28, the milk contained from 80,000 to 100,000 *B. abortus* per c.c. July 8, the blood serum of the goat agglutinated *B. abortus* in dilutions of 1:1,000. The milk contained 20,000 *B. abortus* per c.c. July 17 the goat's serum agglutinated *B. abortus* 1:1,000 and the milk contained about 50 organisms per c.c. August 28, the cultures from the milk were sterile. September 1, tests of the blood serum of the goat were positive in dilutions of 1:600+++ and the milk from the left udder agglutinated *B. abortus* 80 1:100+++. September 27, the left udder was reinfected with *B. abortus*. Milk from the right udder at this time gave positive agglutination tests, 1:100++. October 22, there was no longer any secretion of milk from the udder.

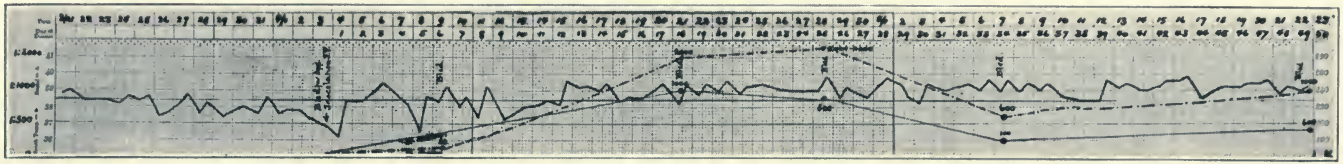

Figure 1

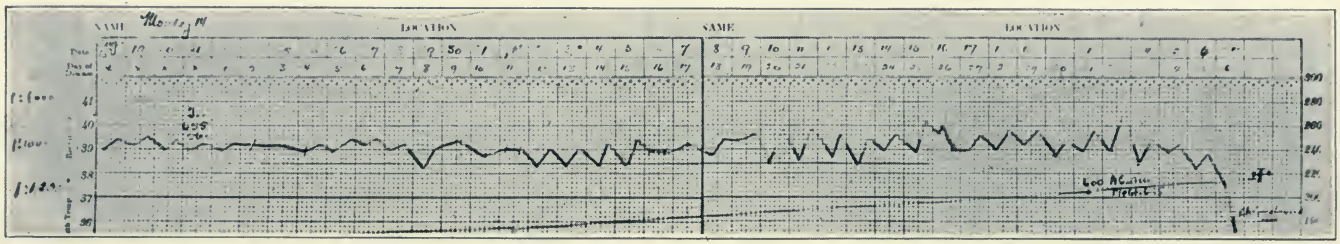

Figure 2

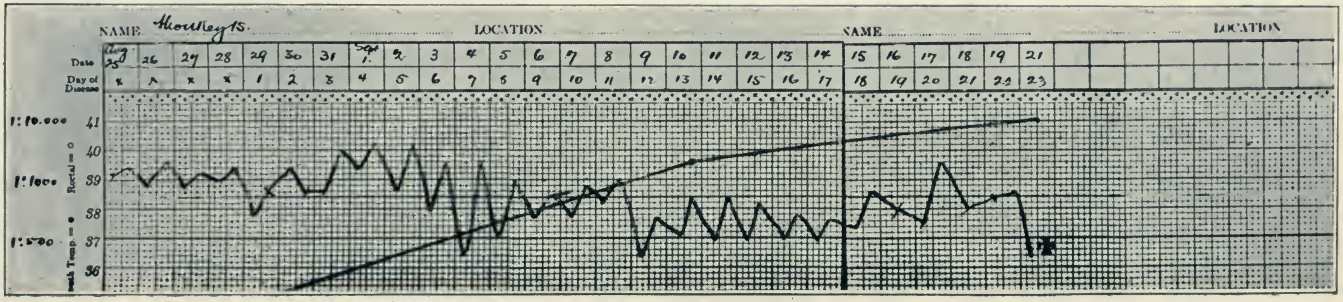

Figure 3

November 8, from bronchopneumonia. (Duration of experiment thirty-nine days.) Cultures from all organs were negative. Agglutination tests negative.

MONKEY 13.—Feeding Experiment. From Aug. 5, to Aug. 24, 1919, fed one slant each of *B. abortus* 80 and 14 on bread or carrots. Aug. 27, 1919, animal was chloroformed. (Duration of experiment twenty-two days.) Necropsy showed a very emaciated animal. Cultures were positive from the mesenteric lymph nodes and spleen. Agglutination reactions were positive: *B. abortus* 80, 1:100+, *B. abortus* 14, 1:100+, and *B. melitensis* 655, 1:100+.

MONKEYS 34 AND 35.—Feeding Experiment. Fed one slant of *B. abortus* 80 and 14. Monkey 34 has shown positive agglutination tests 1:100 on several occasions. Experiment still running.

MONKEYS 36 AND 37.—Feeding Experiment. Have been fed daily pasteurized milk to which has been added *B. abortus* 80 and 14. Agglutination reactions 1:200+++. Experiment still running. Up to the present time have developed no positive agglutinins in the blood.

MONKEYS 38 AND 39.—Feeding Experiment. Have been fed daily pasteurized milk to which has been added one one-hundredth slant *B. abortus* 80. No reaction in the blood. The animals developed a diarrhea, the cause of which up to the present time has not been explained.

MONKEY 40.—Feeding Experiment. From March 30, 1920, for fifty-two days, fed daily the milk of a goat that had been infected with a virulent *B. abortus* recovered from an infected hog. April 23, after twenty-four days of feeding, the milk from the right udder of the goat contained 1,500 organisms per c.c., and from the left udder 250,000 organisms per c.c. May 10, forty days after the beginning of the experiment the milk from the right udder contained 30,000 organisms per c.c., and from the left udder 180,000 organisms per c.c. April 23, after twenty-four days of feeding, agglutination reactions were negative. They were also negative May 7, thirty-seven days after beginning of experiment. May 19, forty-nine days after beginning of experiment, agglutination reactions were positive in dilutions of 1:200. The animal was sacrificed on the fifty-second day. Had lost 300 gm. in weight. The lymph nodes were very much enlarged, a spleen tumor was present and *B. abortus* was recovered in enormous numbers from the spleen, lymph nodes, bone marrow and kidneys. Blood cultures from the heart were strongly positive.

MONKEY 42.—Feeding Experiment. Fed daily milk of a goat which had been infected with hog abortus. Agglutination reactions were positive in the third week. Experiment still running.

MONKEYS 43 AND 44.—Feeding Experiment. Fed one slant of *B. abortus* hog daily. Agglutination reactions with the serum of Monkey 44 were positive in third week. Experiment still running.

In order to prove the melitensis character of the strain of *B. melitensis* which was pathogenic for guinea-pigs, following intratesticular injection, the following two experiments were carried out.

MONKEY 14.—Weight, 2,830 gm. Subcutaneous inoculation. Aug. 21, 1919, was inoculated subcutaneously with strain 655 *B. melitensis*. Nearly dead September 27. Chloroformed. (Duration of experiment thirty-seven days.) Weight, 2,250 gm. Cultures: spleen, 100 colonies; liver, one colony; right kidney, twenty colonies (Fig. 2).

MONKEY 15.—Weight, 2,010 gm. Intravenous inoculation. Aug. 28, 1919, injected *B. melitensis* 655 into right saphenous vein. September 21, comatose. Chloroformed. (Duration of experiment thirty-one days.) Cultures positive from the bone marrow, right and left lung, spleen, urine and liver, *B. meltensis* 655. Agglutination reactions *B. abortus* 80, 1:20,000 + + +, *B. melitensis*, 1:10,000 + + +, and *B. melitensis* 655, 1:10,000 + + + (Fig 3).

CONCLUSIONS

It is not justifiable to draw absolute conclusions from a limited number of experiments, but a careful survey of the data reveals some very interesting probabilities.

1. Following the intravenous injection of *B. abortus bovinus*, agglutinins develop fairly rapidly in the blood of monkeys, and on postmortem it is possible to recover the organisms from the spleen, lymph nodes, liver, kidneys and less frequently from the bone marrow.

2. By feeding agar slants of *B. abortus* on bread or carrots in large and repeated doses, it is possible to get strongly positive agglutination reactions and to recover the organisms from all the viscera at necropsy.

3. By feeding repeatedly the milk of a goat, that has been infected by the injection into the udder of a very virulent strain of *B. abortus* recovered from a hog, it is likewise not only possible to recover the organism from all the viscera, but to determine its presence in the circulating blood.

4. It seems, therefore, justifiable to assume that the *B. abortus bovinus* is pathogenic for monkeys if a virulent culture is fed in large quantities, showing that it has the capacity to penetrate what is apparently a normal mucous membrane of the intestinal tract.

5. In view of the fact that the strain of *B. melitensis*, which produced characteristic lesions in guinea-pigs resembling those of *B. abortus*, when injected into monkeys gave rise in temperature, positive agglutination reactions, and was recovered postmortem in pure cultures from the viscera of the animal, it seems logical to state that this is a true *B. melitensis*.

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THE USE OF FRESH VACCINES IN WHOOPING-COUGH

ROWLAND G. FREEMAN, M.D.
NEW YORK

Vaccines for the prevention or cure of whooping-cough have been used for the past eight years, and while some enthusiasm has been shown by certain writers, the general opinion has been that they were of but little service in the treatment of whooping-cough, although possibly of some value in its prevention. My own attitude was that they did not modify the course of whooping-cough, and I had never seen a case of whooping-cough apparently prevented by their use.

I administered them occasionally, because the parents thought they might do some good, and I knew they would do no harm, but with no more effect than was apparently obtained from drug treatment.

The diagnosis of whooping-cough I have usually confirmed by a blood count, the high lymphocytosis giving one a characteristic picture of this disease.

Two years ago I read Dr. Hueneken's paper on the application of the complement fixation test for the detection of antibodies after the injection of whooping-cough vaccines, in which he showed that the antibodies were not present unless the vaccines were freshly prepared, and that after a week of storage but little antibody production resulted from their injection even in large doses.

It seemed to me possible that this fact might explain the contradictory reports from the use of whooping-cough vaccines, as some clinicians had probably used fresh vaccines by accident in the course of their work. I felt that, at least, this should be tried out, and intended myself to do so in some institution. I regret that I am unable to report any institution work, but I have brought together all the cases in which I have used it in private practice, hoping to stimulate interest in the use of these fresh vaccines and thus render it easier to obtain them, for it requires from one to two weeks to produce fresh vaccines and some cases for which I ordered them have been so far along in the disease by the time they were obtained that one could expect but little effect on the course.

If we are to have an opportunity to give fresh vaccines a fair trial we must have some laboratory producing fresh vaccines every week.

As to the general principle of vaccines being useful in proportion to their freshness I was told by a representative of the Lederle Laboratories in New York, that gonococcus vaccine loses in two days 30 per cent. of its efficiency, and Dr. Fleischner, in the discussion of Dr. Hueneken's first paper, showed that there was some deterioration in the immunizing properties of the tubercle bacillus vaccine on keeping. Dr. William Hallock Park of New York has told me that there is undoubtedly a slow deterioration in all vaccines on keeping; that this deterioration is more rapid in some vaccines than in others.

Immediately after seeing Dr. Hueneken's article I was called to a family with one child who had been coughing for ten days and having paroxysms for a week with vomiting, and a second child who had only begun to cough and who before the first injection had whooped once. A vaccine two weeks old was injected into both children with no material result, but after the first injection of fresh vaccine the youngest child, who was well advanced in the disease, ceased vomiting and had little cough, while the second child did not cough at all after the injection.

A little later I was called to another family where a baby, 8 months old, had had whooping-cough very severely for some time, and for whom the family were very much concerned. In this family also was an older child who had just begun to cough. The baby was materially better after the injection of the vaccines and the other child stopped coughing.

In another case, far advanced in the disease, slight but not material effect from the injections was noted.

Recently I have used these fresh vaccines in a number of cases.

J. M., 6 years old, with two weeks' duration and severe paroxysms, stopped whooping entirely after three injections.

G. W., boy, 4 years old, with very severe vomiting and paroxysms, had a cessation of the vomiting and paroxysms after injections.

W. F., boy, 9 years old, had had paroxysms for a number of days. The vaccines appeared to cure him almost entirely.

S. F., boy, 10 years old, was very materially improved.

E. P., boy, 10 years old, did not have severe paroxysms or severe cough, and did not receive much benefit from the vaccines, the

first dose of which was of vaccine three months old, the second, one month old, and the last fresh vaccine, but this child was well advanced in the disease by this time.

In another family (C.) of two children, aged 7 years and 2 years, respectively, the paroxysms were less frequent and the vomiting stopped, but the vaccines apparently did not shorten the course of the disease.

Very recently I had occasion to use these vaccines in two families, one of six children in which three of the children had recently begun to whoop; and one of three children in which the baby, 2 years old, was having paroxysms. Here we seemed to have a good opportunity for treatment and prophylaxis.

In the family of six children the first injection of vaccine of one-half billion which was twenty-five days old produced no improvement. A second and third injection of fresh Lederle vaccine was also followed by no material change. For the fourth injection I had an absolutely fresh Board of Health vaccine and obtained no material reaction, therefore, no more injections were given and the children were sent to the country. In this family I could not feel that the vaccines had any effect at all. The children who had the disease still had fairly severe paroxysms after the fourth injection, while the three children who were given prophylactic injections developed whooping-cough although not of a severe type.

In the other family of three children, after the first injection of one month old vaccine in the child who was having paroxysms, no more paroxysms were observed, and the other two children have never coughed since.

SUMMARY

To summarize: in sixteen children with whooping-cough in which the vaccines were used at various periods of the disease, in five no results were obtained. Of these five children three were early in the disease and the other two very late.

Of the eleven remaining cases, in nine a very material improvement took place and in four of these a practical cure was obtained.

Of the five cases in which prophylactic doses were used two were successful and three failed.

My confidence in these vaccines has been somewhat shaken by the results in this family of six children who failed to react, but the good results obtained in other cases and the quite remarkable results obtained

in certain beginning cases convinces me that these vaccines should have an extended use, particularly in institutions, where controls may be used to demonstrate whether we may not have in these vaccines a valuable method of reducing the large mortality from whooping-cough.

The dosage used in all the above cases was 500,000 for the first dose, 1,000,000 for the second dose and 2,000,000 each for the third and fourth doses.

DISCUSSION

DR. HUENEKENS: Dr. Freeman referred to the complement fixation test. That consists in the injection of vaccines and then testing for the complement. In fresh vaccines one gets from 90 to 100 per cent. positive complement fixation tests; when the vaccines are four months old one gets practically no positive reactions. When we use fresh pertussis vaccines it is thus shown that the body is attempting to produce antibodies, but whether enough are produced to affect in a marked degree the pertussis is another question. If we are going to use vaccines at all in whooping cough we had better use fresh vaccines. Conclusions drawn from clinical observation alone are open to criticism. However, in my own experience in about 10 per cent. of the cases the results are dramatic; in another 10 per cent. there are practically no results whatever, while in 80 per cent. there seems to be a decided benefit, enough to warrant giving the vaccines early but not after the disease is at its height; I do not feel that it is safe to draw conclusions at this time as the disease may be on the decline and improvement might take place whether vaccines were given or not. In St. Paul and Minneapolis we are now furnished with fresh vaccines on twenty-four hours' notice and since this has been possible we are using them more and more.

DR. FREEMAN: I apologize for the small series of cases. I have presented this paper to stimulate interest in the use of fresh vaccines so there will be a demand that will make them obtainable promptly when we want them.

CASE OF SARCOMA OF THE KIDNEY

ROWLAND G. FREEMAN, M.D.

NEW YORK

This case of sarcoma of the kidney is of interest because, while the type of the tumor on microscopic examination corresponded with another case submitted to operation in the hospital and which had not recurred in five years, in this case metastasis in the lungs developed very rapidly, and caused the child's death.

REPORT OF CASE

The child was brought to my office with a history of failing health for two months, the bowels were sometimes constipated, at other times loose with a watery mucus feces, there was anorexia, emaciation, and fever at times, and pain in the back and in the abdomen, and occasionally vomiting. For a week she had had a cough. She was 2½ years old and weighed 26½ pounds.

Nothing definite was made out on examination because the child was crying, but she was sent to The Roosevelt Hospital, where, when the abdomen became relaxed, a definite abdominal tumor was easily mapped out in the left side of the abdominal wall, which was spherical in shape and which corresponded to a sarcoma of the left kidney. Roentgen-ray examination corroborated the diagnosis, and the child was operated on a week after admission.

After removal of the kidney the child had a febrile reaction which passed off in five days, after which the temperature remained below 100 F. until three weeks after operation, when it was arranged that she was to be taken home. However, at this time she had a rise of temperature to 101 F. and on examination fine râles were found to be present over the left lower lobe. The following day there were also fine râles over the right lower lobe and the temperature was still higher, but two days after this the temperature was normal and three days later the child was discharged, the signs over the chest having disappeared.

During the child's stay in the hospital her weight had neither increased nor diminished.

Sixteen days after her discharge from the hospital she was brought to my office with a temperature of 102.5 F., rapid breathing, many fine râles over chest on both sides, apparently in a grave condition, and another roentgen ray of the chest was taken. The child returned home and died two days later, less than two months from the date of operation.

The last roentgenogram showed large tumor metastases in both lungs with no evident abdominal abnormality, except a large spleen.

The question as to when this process in the lung began is of interest. There is the possibility that it may have begun on the date the child was to leave the hospital and began to have fever, but the roentgeno-

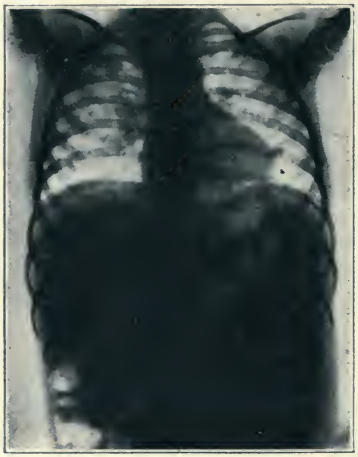

Fig. 1.—Sarcoma of kidney, on admission to hospital, showing marked hilus shadow and slight mottling of lung.

Fig. 2.—Same case as shown in Figure 1, nearly two months later with kidney removed. The lung contains characteristic metastases.

gram of the chest taken when the child was admitted to the hospital, in view of what occurred later, leads me to suspect that what we took to be a hylus shadow was the beginning of metastases in the lungs which was not sufficiently definite to give a characteristic shadow. On the other hand, it is possible that what was seen in the first roentgenogram was an ordinary hylus shadow and that the invasion of the lung began when the rise of temperature occurred on the day on which it was intended to discharge the child from the hospital.

DYSPITUITARISM SO-CALLED: ABSORPTION OF MEMBRANOUS BONES, EXOPHTHALMOS AND POLYURIA

REPORT OF TWO CASES

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PHILADELPHIA

In the Transactions of the Pathological Society of Philadelphia,[1] under the heading, General Tuberculosis, and also in the Archives of Pediatrics,[2] under the caption, Polyuria and Tuberculosis, I made the following report, exhibiting the specimens to the Society:

Dec. 1, 1892, a boy, aged 3 years, was admitted to the Children's Hospital with a history of great thirst and polyuria which had begun suddenly eight weeks before. He had had enterocolitis at 5 months of age, and croup and measles together when 2 years old.

The family history was negative, the parents, three brothers and two sisters being alive and well; one younger sister died of enterocolitis. There had been no miscarriage.

The examination showed the boy to be undersized and puny, with light hair, brown eyes and a bronzed, dry skin. The eyes were in a condition of exophthalmos, giving him a froglike appearance, and there was a corneal opacity on each eye, with anterior synechiae in the right. The thyroid was not enlarged. His chest was very small and narrow and the rachitic rosary could be felt. The lungs and heart were normal. His belly was distended and tympanitic, obscuring for several days the great enlargement of the liver and spleen, which at first were thought to be normal in size; there was an umbilical hernia and the skin of the abdomen was covered with petechiae and an eruption something like scabies. The feet were edematous.

The urine had the following characteristics: acid, cloudy; specific gravity, 1.000; quantity in twenty-four hours, 114 ounces; no sugar; albumin distinct.

The boy seemed to suffer so much from thirst that water and milk were not withheld, and he was given a drink whenever he asked for it. He was at once put on two minims of the fluid extract of ergot, three times daily. This had no effect whatever, at the end of a week the daily amount of food ingested being 180 ounces, of which 150 ounces passed through the kidneys without taking up either albumin or sugar, the specific gravity not rising above 1.000, but the color being like that of a saturated solution of picric acid. During this week the temperature had been rather irregular, but there was no decided fever until the seventh day, when the thermometer registered 102.2 F. The ergot was now replaced by laudarum, 2 drops every six hours. Before this

1. Tr. Path. Soc. of Phila., **116,** 1891-1893.
2. *Arch. Ped.,* **10,** 1893.

the thirst had not allowed more than a few minutes' sleep at a time, but the boy now began to take longer naps and the amount of fluid taken fell to 100 ounces.

During the next week the urine contained albumin once, but at the end of that time it was free from it, had changed to pale yellow in color, and had a specific gravity of 1.010. After this the total amount could not be collected, so an idea of the amount voided could only be gained by measuring the quantity of water and milk drunk, which decreased to about 80 ounces. December 20 the urine had its highest specific gravity, 1.012, but the next day it fell to 1.004. December 22 the temperature rose from 99 F. in the morning to 105 F. at 4 p. m. It was normal on the twenty-third and at 6 a. m. of the twenty-fourth, but at noon it was 103 F. The opium was then stopped and one grain of quinin given, three times a day, with a very beneficial result. The temperature for six weeks did not vary a degree from normal, the liver and spleen decreased in size, the petechiae on the abdomen gradually faded, the boy was able to get up and walk, and he ate and drank no more than a child of three years should.

February 12, at 6 p. m., the temperature was 99 F.; four hours later it had risen five degrees. After a few days a bronchopneumonia was discovered, and a further diagnosis was made, from a general view of the case, of tuberculosis. For a week the temperature was very irregular and there was marked systemic depression. On the nineteenth the purpuric spots increased in number and an elevated, dull-red macular rash appeared all over the body and extremities. At 8:30 p. m. he sat up and asked for a drink. Two hours later the body was cold and rigor mortis had set in.

The necropsy was made fifteen hours after death. The rash had faded from the left side, but still persisted on the right. As the scalp was stripped off, a yellow spot about the size of a five-cent piece was noticed near the right parietal eminence. When the skull cap was removed this spot was seen on the inner side as well, and the entire thickness of the bone was soft and movable. Other smaller areas not extending through the vault were seen on the outer surface. In the absence of any history of syphilis these were thought to be tuberculous. The brain was normal to macroscopic examination. The lymphatic glands in the omentum, mesentery, mediastinum and, in fact, all through the body were greatly enlarged. There was a bronchopneumonia of both lungs, a warty endocarditis of the mitral valves and a caseous pleuritic adhesion at the base of the right lung. The liver and spleen were enlarged and firm and the former had minute gray nodules in its substance. The pancreas was apparently normal, and there were no ulcers or scars in the intestines. The kidneys seemed slightly enlarged; the left contained three cysts, and in the pelvis of each was a yellow, hard tubercular mass, almost filling it. Microscopic sections prepared by Dr. W. S. Carter showed nodular masses of small round-celled infiltration in the liver, spleen, kidneys (pelvis), a bronchopneumonia in the lungs, and a degeneration of the epithelium of the uriniferous tubules.

Subsequent experience at the postmortem table, with a large percentage of the cases showing tuberculosis but without duplicating these features, made me begin to doubt whether the tuberculosis in this case had any causal relation to the triad of symptoms described, and this doubt was further strengthened by seeing in 1905 a patient presented

to the Medical Society of the State of Pennsylvania by Dr. Thos. W. Kay and reported by him [3] under the title, "Acquired Hydrocephalus with Atrophic Bone Changes, Exophthalmos and Polyuria (with Presentation of the Patient)." The report is of such interest that I quote it in full:

R. S., male, 7 years of age, and only child of healthy parents. Up to 4 years of age he was healthy and well grown as shown by photograph. He was attacked by scarlet fever at that age, which was followed by a discharge from the right ear which still persists. Four months after scarlatina he had vertigo and cried occasionally with pain in the head. About this time enlargement of the superior cervical and submaxillary glands took place, which was most marked on the right side. These glands are still enlarged, but give no discomfort. Five to six months after the scarlatina the gums began to separate from the teeth and this was followed by a gradual loss of most of the teeth, beginning with the molars. About the same time the mother noticed a soft spot on the head, which side she does not remember, where there seemed to be no bone. Eighteen months ago exophthalmos began to make its appearance and has been getting steadily worse. Now it is so bad that the eyes have to be protected by wearing a handkerchief over them as they are too prominent for the use of glasses. Fourteen months ago polyuria appeared and he would void his urine, in small quantities, two hundred or more times in twenty-four hours. Now he micturates several times an hour and as much as twenty-seven ounces at a time is passed. Its reaction is neutral and the specific gravity is from 1.000 to 1.001. Seven months ago he weighed 32 pounds and he passed 27 quarts of urine daily (54 pounds). Now he weighs 36 pounds and he passes 23 quarts daily (46 pounds). The bones of the body with the exception of the lower jaw and the bones of the cranium are comparatively normal. The lower jaw has lost its bone salts and the resultant cartilaginous mass, containing one incisor, has been so deformed by the depressor muscles that the chin has disappeared. The circumference of the cranium is 53 cm., the right side being slightly larger than the left. The squamous portion of the right temporal bone gives readily to pressure with the finger. The right parietal bone has in large part been absorbed, leaving an irregular 6x7 cm. oval opening. The left parietal bone has been nearly entirely absorbed, leaving an irregular 9x11 cm. opening. The frontal bone has suffered on the left side, resulting in an irregular 4x5 cm. triangular opening. The bone at the sites of the fontanels and sutures is not affected. When I first saw the patient some seven months ago the openings in the bones were not as large by 1 cm. in diameter as now. The patient is irritable but fairly bright and the organs of special sense and the rest of the body are in as good condition as could be expected. Whether awake or asleep his breathing is somewhat stertorous. Of course with polyuria there is a corresponding polydipsia. The causative lesion in this case is situated, most likely, in or about the floor of the fourth ventricle.

Bearing these two cases in mind, it was with interest that I saw in the prospectus of the Osler Memorial Volume the title of an article by Henry A. Christian, "Defects of Membranous Bones, Exophthalmos

3. Pennsylvania M. J., **9**, 1905-6.

and Polyuria, an Unusual Syndrome of Dyspituitarism," and I hoped that the solution of these two cases had been reached. Dr. Christian's report is very thorough, giving the results of a careful study of his patient during a stay of six months in the hospital. The patient is a girl who was well up to 3 years of age, when the teeth began to decay and the gums became sore; exophthalmos began at 3½ years, with increasing thirst and polyuria. When studied at the age of 5 years the roentgenogram of the skull showed extensive defects in the bones, and similar but slight changes were also found in the ilium and ischium. Two similar cases were found by Dr. Christian in a search of the literature, reported by Schueller [4] under the title, "Ueber eigenartige Schaedeldefekte im Jugendalter," one, a boy 16 years old, with dystrophia adiposogenitalis, showing exophthalmos and defects in the bones of the skull, but no polyuria; the other, a 4-year-old girl, whose exophthalmos and bony defects began at 2 years of age, the thirst and polyuria developing, at what time is not stated. Schueller's report of this case closes with the statement, "We can therefore make a presumptive diagnosis of anomaly of the skeleton as the result of disease of the hypophysis." Dr. Christian treated his patient with pituitary extract, and when this was given under the skin or into a vein, a great lessening was seen in the amount of fluid ingested and excreted, but administration by mouth or by rectum had no effect. He, therefore, concludes that the syndrome is probably due to disturbed pituitary function.

Two weeks after I had received the prospectus of the Osler Memorial Volume, and while waiting eagerly for its publication, there was brought into my office by Dr. L. F. Luburg a boy 4 years old, from whom there had been removed at 2 years of age a tumorlike swelling in the left parietal region, absence of the bone beneath it down to the dura being noted; the pathological report on the tissue removed was "no gumma; no sarcoma; slight degree of inflammation; mainly myxomatous change." Since then other swellings have appeared, and exophthalmos, greater on the left side, has taken place, but as yet no polyuria. The boy was very irritable and objected to being examined, so it was possible to make only a brief examination, which was negative, except for enlargement of the cervical glands. He was then taken to the Methodist Hospital, where the blood and urine were examined

4. Fortschritte a. d. Gebiete der Roentgenstrahlen, **23**:12, 1915.

without showing anything unusual, and skiagraphs of the skull taken, which are here presented through the courtesy of Drs. Luburg and Percival. The boy was so restless and irritable that it was a difficult matter to get satisfactory plates, but they all show the large areas in the calvarium without bone and, overlying these the mounding up of the scalp; one of the plates gives a clear-cut view of the base and shows the sella turcica to be uninvolved in the bone change, differing in this point from the illustration in Dr. Christian's report in which the sella turcica is decidedly affected. The patient was then taken to his home in the interior of Pennsylvania, where he is still (May, 1920) living.

To explain the origin of these cases, the theory of dyspituitarism is a very captivating one and receives partial confirmation from the action of pituitary extract in Dr. Christian's case. But after a review of the works of Sajous, Gley and Schaeffer on the physiology and known pathology of the endocrine organs, and also after an analysis of these six cases, it seems to me that there are several objections to that theory. But let me hasten to state that I agree with Dr. Christian that the polyuria depends on disturbed hypophysis function, as will be explained later. And I also agree with him that the condition does not seem to depend on syphilis.

The objections to the theory of dyspituitarism are:

1. Two of the cases have not shown any polyuria.

2. In two of those having polyuria, and probably in all four, the exophthalmos and the bone changes came first.

3. Injection of pituitary extract, although diminishing the polyuria, had no effect on the bone changes.

4. The exophthalmos is probably not of toxic or endocrinic origin, but, as Schueller suggests, is mechanical, due to involvement of the orbital plate of the frontal bone, as shown by the four who have been studied by the roentgen rays.

5. The changes in the bones, as suggested by Dr. Percival, are not such as would most likely be produced by a chemical substance which ought to affect the bones in their entirety; but these changes start in a number of different foci, as though some solid bodies were carried to the bones in the blood supply, and lodging in the medulla or periosteum set up their action there. In confirmation of this is the observation in my first case that in some areas only one table of the bone (the outer) was affected.

6. As mentioned above, the polyuria probably depends on disturbed function of the hypophysis, this disturbance being due to pressure from changes in the bone in the immediate neighborhood of the gland; thus, in the two patients who have not had polyuria (Schueller's first and my second case), the roentgen rays showed the sella turcica to be unaffected, while in the other two who had been skiagraphed (Schueller's second and Christian's, both having polyuria) decided changes were shown in the sella.

OTHER THEORIES

Dr. Percival made the remark, while examining the plates with me, that their appearance is typical of osteosarcoma, but that this can be excluded by the duration of life in most of the patients. This suggests, as one possible explanation, that the primary process may be neoplastic, benign and myxomatous in character, affecting for some unknown reason the membranous bones, and producing exophthalmos and polyuria secondarily by pressure.

Another thought, that of a chronic infectious process, is raised by the presence in two of the cases of prolonged suppuration (discharging ear) and in three cases of enlargement of the lymphatic glands. But these enlarged glands may be only part of a general lymphatic enlargement, with an enlarged thymus, which brings us back to the endocrine theory again, but referring it this time to the thymus, about which so little is known. It is known to have some influence on the development of the skeleton, and some disturbance of it is supposed to be associated with achondroplasia, but, strangely, in that condition the membranous bones are found to be uninvolved, so that this theory seems unlikely.

With the possibility of this being an infectious process and since at least two of the cases seemed to start with decay of the teeth and inflammation of the gums, the thought occurs that the infective agent may gain entrance through these structures and may be animal (ameboid) rather than vegetable in character. This theory also offers an explanation for the apparent benefit in my first case following the use of quinin.

Further observations are needed before this curious and interesting group of symptoms can be satisfactorily explained.

THE FACTOR OF THE POSITION OF THE DIAPHRAGM IN ROENTGEN-RAY DIAGNOSIS OF ENLARGED THYMUS*

H. J. GERSTENBERGER

CLEVELAND

The diagnosis of the presence of an enlarged thymus by percussion I believe has been considered by most physicians to be a difficult and uncertain performance. Therefore, the advent of roentgen ray was hailed and is generally still believed to be a safe and dependable diagnostic method as applied to the thymus.

An experience during the past winter has convinced me that the diagnosis of an enlarged thymus with the aid of the roentgen ray is also liable frequently to be very uncertain and to be a source of erroneous interpretations and findings.

A brief recapitulation of this experience will bring out the interesting points.

REPORT OF CASE

In July, 1919, in the absence of the family physician in the army, I was called to attend the child of a colleague, whose skin was scaly and itchy and who was breathing with difficulty. The boy, 12 months old, was quite well developed and nourished, showed a mild rickets, a distinct but slight eczema of the face, chest and arms, causing a great deal of itching, and a decided emphysema, accompanied by wheezing and a somewhat labored expiration. The spleen was not palpable and the posterior cervical lymph nodes were somewhat increased in size and in number, as is usually the case in exudative children.

The child had since his third week received a Walker-Gordon mixture, and recently has been given straight cow's milk and vegetables.

The condition was considered to be due either to a hypersensitiveness to some food constituent or to an exudative diathesis.

A skimmed milk diet, atropin sulphate in increasing drop doses, to physiologic limit, and 10 per cent. tricalcium phosphate in cod liver oil was ordered, and was followed by a decided improvement.

During August, 1919, the family physician returned, found an increased thymic dullness, and requested a roentgenogram, which showed a wide shadow, especially to the right but also to the left of the sternum, and which the roentgenologist stated was caused by an enlarged thymus. Consequently the family physician stopped the atropin and had the thymus exposed every three to four weeks for a total of five exposures.

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* From the Departments of Pediatrics of Lakeside Hospital and of Western Reserve Medical School.

The condition of the child, however, grew slightly worse instead of better, and the thymic shadow remained the same, so that the roentgenologist advised against further exposures. The family physician then reordered the atropin in the form of belladonna in small doses. The child improved again and breathed in a nearly normal manner during the latter half of November, 1919.

During the first days of December he contracted a cold and in the night of December 3 he became severely asthmatic and somewhat cyanotic. I saw him with the family physician December 4 and he was then taken to Lakeside Hospital for diagnosis and treatment.

Nov. 10, 1919, the family physician had his assistant make cutaneous scratch tests with different proteins in simple saline solution, which were all negative. The proteins used were as follows: wheat, cow's milk, rice, potatoes, egg white, beef, oats, tomato, horse hair, pneumococci, staphylococci and ragweed.

December 4 at the hospital the diet and therapy of July, 1919, were reordered and the child improved.

December 5 a roentgenogram was taken, which showed a much smaller shadow than had ever been seen in this case before and really one that was practically normal. This finding convinced the family physician that after all the improvement noticed in the latter half of November, 1919, was due to a reduction in the size of the thymus, which had occurred since the last picture had been taken in October.

Intracutaneous sensitization tests were carried out at the hospital from December 8 to 13 and showed the child to be negative to cow's milk casein, cow's milk albumin, strawberry, orange and tomato, questionably positive to cow's milk allergen and enormously sensitive to egg yolk allergen and egg yolk albumin. The latter two tests were accompanied by a severe anaphylactic shock that was relieved by the administration of adrenalin subcutaneously.

December 16 two roentgenograms were taken, both of which showed an abnormally large shadow in the thymic region, in other words, just the opposite from the last findings in the plates of December 5.

The improvement of the child, that was still getting atropin in increasing doses, cod liver oil with calcium phosphate and skimmed milk, continued, and did not correspond with the decided reversal in the shadow in the roentgenogram.

A fluoroscopic examination was immediately made and succeeded in establishing the interesting fact that the two extremes of normal narrow shadow, on the one hand, and a markedly wide and seemingly abnormal thymic shadow on the other, corresponded in the former with the end of a deep inspiration and in the latter with the end of a deep and forceful expiration.

The development of the shadow in its most marked form under the fluoroscope may well be compared with the filling of miniature lungs which paradoxically decrease in size with inspiration and collapse entirely with a deep taking in of air. In order, however, to get this markedly increased shadow which in this patient was always greater on the right than on the left and frequently present only on the right side, especially if the expiration had not been of the extreme type, it was necessary to have the child cry vigorously and establish a prolonged and forceful expiration.

It is especially significant to note that the expiration had to be forceful, for at times I saw a prolonged expiration produce an increase in the shadow of the thymic area without presenting the beautifully clear picture to either side of the vertebral column, simulating as stated above the filling to capacity of a miniature pair of lungs with distinct outlines, definite and sharp borders. Whenever I have seen this picture produced under the fluoroscope it has seemed to me

that the diaphragm moved distinctly upward and was directly or indirectly responsible for it. Likewise, I have always seen a distinct descent of the diaphragm, accompanied by a very deep and very voluminous taking in of air, precede the rapid and complete disappearance of the abnormal shadow.

Unless this deep inspiration and distinct drop in the position of the diaphragm occurred, the shadow would only get smaller and indistinct as it partially receded toward the middle line.

Whenever a clear and marked shadow was seen under the fluoroscope one could note the outlines of the lobelike shadow on either side, but again always more distinctly on the right than on the left, and a definite and sharp but slightly rounded angle at the extreme outer and lower pole, separated by a clear rather straight space from the heart and distinctly away from it and pointing out into the area of the lungs.

At no time was any pulsation noticed in any of the shadows or in any part of a shadow, when seen under the fluoroscope in this patient.

It is further significant that only when a forceful expiration was established could a lobelike shadow be seen to the left of the middle line and then never as clearly as on the right side. When the shadow on the right side was medium in degree no definitely outlined form could be seen on the left side. All of these pictures were seen much better in the fluoroscope than in the roentgenogram. However, on three of the pictures a less intensive, lobelike somewhat hazy shadow can be seen to the left of the middle line, which together with the shadow on the right side sits over the heart in the form of a blunted cone with a distinct lower border separated at the side, especially on the right side of the heart, by a clear sharp space as described above, and forming a distinct angle, pointing outward and away from the heart.

The child went home for the Christmas holidays and returned to the hospital January 7, where it remained for ten days. During this time four attempts were made to register on plates in prompt and, if possible, in immediate succession pictures of the two extremes seen with the fluoroscope, so as to be able to present to those interested in the roentgen-ray diagnosis and therapy of the thymic gland, the customary before treatment and after treatment pictures only obtained, however, in this child both on the same day and at the same sitting.

January 8 both plates showed wide shadows to the left as well as to the right, but much more distinctly on the latter side.

January 12 it was again impossible to obtain photographs during the height of inspiration and both plates showed in consequence decided shadows to the right.

The pictures taken January 15 were out of focus and could not be utilized.

Finally January 17 we were able to get first a markedly wide shadow involving both sides and immediately afterwards a narrow shadow that was practically normal and just like the two obtained December 5. In other words, we did obtain in the same child at the same sitting both a normal and an abnormal shadow in the thymic region, certainly a difficult finding to interpret.

COMMENT

Numerous questions difficult to answer immediately arise. Is this shadow due to the thymic gland or to something else as the superior vena cava or the right auricle? Is the thymus really abnormally large

or is its size actually within the variable normal limits, and is it brought into the plate in the form of an abnormal shadow simply as a result of the operation of some other abnormal factor such as an abnormally increased intrathoracic pressure especially in this child, whose lungs, owing to a possibly at times still existing constriction of the bronchials, might retain more air than those of a normal child at a given stage of respiration and so might enable the production of an intrathoracic pressure in forced expiration that would be greater than that found in a normal child?

Or are the intrathoracic factors causing the thymus to stand out in this so-called abnormal manner really normal and simply abnormally utilized in the sense of hypereffectiveness?

For instance, is it possible that one normal child can push his diaphragm up more effectively or increase his intrathoracic pressure more decidedly than another normal child of the same age and weight? Again, if it is the thymus are its lobes mechanically pushed upward and outward by the ascent of the diaphragm or are they enlarged by a sudden filling with blood as a result of the establishment of an abnormal disproportion between the outflow and the inflow of blood into the gland? Or is its coming out into view due only slightly to the possible effect of the vascular supply on the thymus and mainly due to a following of a mechanical path of least resistance, as a result of a markedly increased intrathoracic pressure produced by various factors, but recorded best by the ascent of the diaphragm? Does the varying topographical relation of the lungs to the thymus play a part?

Why is the shadow more often present on the right side, and when also present on the left, less distinct than on the right? Is this shadow on the right side really due to the thymus or is it produced by the superior vena cava and right auricle? If it is produced by the thymus is it caused by its close proximity to the just mentioned venous structures? Or is it due to possibly more rapid enlargement of the right lobe than of the left lobe of the thymus, or is it mechanically advantageous under an increased intrathoracic pressure for the right lobe to move out before the left?

Is such a freedom of mechanical mobility of the lobes within the sac of the thymus possible, or is it necessary that a force from within such as would be represented by the filling of the thymus with blood be developed to force the lobe outward in the manner observed?

These questions are all of importance, and I do not see how we can answer them with positiveness until further data are at hand. Definite contradictions exist in the literature regarding most of these points. I have been unable to find satisfactory data regarding the blood supply of the thymus, especially regarding the proportion existing between the inflow and outflow.

Rehn,[1] Hotz [2] and Hart all think that the exit venous channels are relatively better developed than arterial inflow vessels, and yet Klose,[3] notwithstanding the fact that he quotes Hotz and Hart as his authorities, expresses just the opposite view, based mainly on the findings of Siegel,[4] who reported in one case the presence of a network of fine veins on the circumference of the gland and the absence of larger venous channels. Siegel, however, does not attach the same generalization and significance to this individual observation.

Rehn, in 1906, observed at operations on the thymus a regular downward movement of the thymus with inspiration and an ascent with expiration. He makes the further comment that the more forceful the inspiration or expiration the greater the descent of the thymus in the one instance and the ascent in the other, and with deep inspiration the thymic gland is aspirated as it were into the thorax, whereas by severe expiration as during crying, coughing, the gland is forced up out of the chest.

Rehn claims that this physiologic up and down movement of the thymus is responsible, when it is enlarged, for the difficulty in breathing that is noticed in some cases at beginning of inspiration, by fitting better and more snugly in the upper opening of the chest and so acting as a more tightly fitting valve.

Benjamin and Goett,[5] in presenting their experiences at Pfaundler's clinic with roentgen-ray studies of the thymic gland in infants, report an exactly similar observation as the one made by me in this patient, with this difference, however, that the shadow, as observed under the fluoroscope, increased with the descent of the diaphragm and decreased

1. Rehn, L.: Die Thymusstenose unter der Thymustod, Verhandl. d. Deutsch. Gesellsch. f. Chir., April, 1906, 35th Congress, p. 364.
2. Hotz, G.: Die Ursachen des Thymustodes, Beitr. z. klin. Chir. **55**:515, 1907.
3. Klose, H.: Beiträge zur Pathologie und Klinik der Thymusdrüse, Jahr. f. Kinderh. **78**:653, 1913.
4. Siegel: Berl. klin. Wchnschr., No. 40, 1896.
5. Benjamin, E., and Goett, T.: Zur Deutung des Thoraxradiogramms biem Säugling, Deutsch. Arch. f. Klin. Med. **107**:509, 1912.

with the ascent. They come to the provisional conclusion that the abnormal picture was produced by the distention of the vena cava and not by the thymus. Later on in their article, however, they modify this conclusion by stating that, according to their recollection, the child cried at the time when the picture of the abnormal shadow was obtained, and was quiet when the good shadow was procured.

If their provisional conclusion is the right one, then the interpretation given by them would seem to be correct from a physiologic point of view. But, as they remark, there is no uniformity of opinion in the literature as to whether the heart in adults during inspiration is wider or smaller than it is during expiration, or vice versa.

Grödel [6] and Dietlen [7] are of the opinion that the descent of the diaphragm produces an inspiratory narrowing of the cardiac shadow, and that the ascent produces an expiratory widening, while Holzknecht and Hofbauer (quoted by Benjamin and Goett) find a widening of the shadow during the entire inspiration.

Dietlen bridges the two contradictory views by admitting a widening of the cardiac shadow in early inspiration due to the sudden filling of the superior vena cava and right auricle as the result of the suction effect during the early part of inspiration.

Benjamin and Goett also quote d'Oelsnitz and Paschetta [8] as having called attention to the part played in infants by the large vessels in the widening of the shadow at the base of the heart and to the fact that this widening is influenced by respiration in the sense that the shadow becomes wider in expiration and narrower in inspiration.

In addition these authors further claim that an enlarged thymus appears mainly to the left of the vertebral column. So one can readily agree with Benjamin and Goett that a subject that at first glance seems simple and clear, when viewed from the standpoint of opinions as written down in the literature, is complicated and difficult.

Benjamin and Goett were checking Hochsinger's [9] claim that the stridor congenitus was caused by the presence of an enlarged thymus,

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6. Grödel, F. M.: Röntgenkinematographische Studien über Herzgrösse und Herzlage, Ztschr. f. klin. Med. **72**:310, 1911.

7. Dietlen, H.: Ergebnisse des medizinischen Röntgenverfahrens für die Physiologie, Ergebn. d. Physiol. **10**, 1910.

8. d'Oelsnitz u. Paschetta, Bull. de la Soc. de Pediat, Paris, 457, 1911. Quoted by Benjamin u. Goett, Deutsch. Arch. f. Klin. Med. **107**:514, 516, 1912.

9. Hochsinger: Stridor thymic. in fant, Wien. med. Wchnschr., No. 45, 1903; No. 33, 1910.

and that this enlarged thymus could be found in the roentgenogram. They had occasion to perform a necropsy on a 7-months-old infant killed in an accident and who also had a congenital stridor and of whose thymic area a roentgenogram had been made. A 20 gm. thymus was found and neither was it nor any other gland in the place where a shadow had been obtained in the plate. This fact, of course, does not prove that the thymus was not concerned in producing the shadow during life.

Again in another infant, the child of a wet nurse, who had never had a congenital stridor but who had frequently showed in the roentgenogram the presence of Hochsinger's shadow and on whom a necropsy was made after an acute illness of six days' duration they found only a very small thymus weighing hardly 3 gm., and conclude that it could not have been a factor in the production of the shadow in this child.

It is well to remember in this connection that Benjamin and Goett found their shadow, as observed under the fluoroscope, during inspiration and not during expiration, and therefore they could hardly expect the thymus to be a factor unless it be of enormous size.

Benjamin and Lange [10] state "that the breadth of the upper mediastinal shadow varies normally with the age and general condition of the patient, and since it may vary from time to time in the same patient the roentgen-ray diagnosis is not always easy or free from error." They continue further, "in one case not included in this series an apparently normal shadow was obtained when the child was quiet or sleeping, but during a restless crying spell the thymic shadow became greatly enlarged.

"The roentgen-ray shadows of congenital heart enlargements are often confused with thymic enlargements. In all cases in which the roentgen-ray diagnosis seemed doubtful, a roentgen-ray exposure was given as a therapeutic test and this test has proven very reliable."

In other words, Benjamin and Lange have made an observation similar to mine by getting a wide shadow in a crying child—picture in all probability taken in decided expiration—and a normal shadow while the child was quiet and sleeping—picture probably taken in inspiration or in very superficial expiration.

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10. Benjamin, J. E., and Lange, S.: Report of Nineteen Cases of Hyperphasia of the Thymus Gland, Treated by the Roentgen Rays, Arch. Pediat. **35**:71, 1918.

These authors do not, however, indicate how they decided in this case by therapeutic tests or otherwise, whether the infant had an abnormal thymus or not as this child was not a part of the series which they were reporting. Nor do they go into the possible rôle that respiration or the diaphragm might play in the production of this shadow picture.

It would seem as if the therapeutic roentgen-ray tests based on finding a normal shadow would be valueless unless checked by observations made at two different respiratory phases and especially with the aid of the fluoroscope.

The patient forming the basis of this contribution is an excellent example of the case in point. Here we have a boy who has a history of difficult breathing, especially during expiration, accompanied by slight cyanosis, symptoms which very well fit into the picture of a case of so-called thymic asthma, just as they also may be just as well a part of the clinical picture of a child sensitive to proteins, or of an exudative child with asthma. Although he has received sufficient exposures to the roentgen ray, this boy can show, just as you wish, either a normal or an abnormal shadow of the thymic region, corresponding with marked inspiration in the former, and with deep and forced expiration in the latter, but not running parallel to his general condition.

This patient has a definitely abnormal shadow that, in all probability, is produced by forcing the thymus upward and outward, and yet it is also most probable that this thymus is not mechanically concerned in giving him his respiratory difficulty. And in the face of a marked protein hypersensitiveness, accompanied by a mild eczema and expiratory asthma, it is impossible to claim that this boy is one of the thymic cases that are refractory to roentgen-ray therapy and that for this reason his thymus gland has not decreased in size. In other words, unless we find in this boy what, at the present time is considered to be a normal shadow, both in expiration as well as in inspiration, under the fluoroscope, as well as in the roentgen-ray plate, we will not be able to give credit for his improvement to the effect of the roentgen ray on the thymus gland.

Of course seemingly definite cases of clinical thymic asthma in the newly-born have been rapidly and definitely relieved of their symptoms by exposure to the roentgen ray. Usually their improvement has been accompanied by decided narrowing of the shadow, so that the conclusion has been drawn that the betterment was due to the reduction in size of the thymic gland. But in the light of the present case under

discussion we cannot be sure that the roentgen ray actually reduced the size of the gland and still it really may have accomplished just that. Further observation on the basis of the experience attained with this patient will help to settle that question. It may be that as a result of the exposure to the roentgen ray the child's condition was improved, and as a result he was more quiet when later pictures were taken, so that normal shadow may have been produced because the child was more comfortable and did not cry and squirm when the pictures were being taken, rather than because the thymic gland had been decreased in size.

It is necessary to call attention to one of the arguments used by Benjamin and Goett in favor of their opinion that the abnormally wide shadow found in normal children varies according to their condition; the well nourished showing a wide shadow, the poorly nourished a normal shadow. They attributed the variations to the difference in blood volume between the two types of children. While this difference does exist, it is equally true that the size of the thymus gland seems to follow the same rule, being small in the skinny child and large in the well nourished, so that this argument can be applied to one theory with no greater justification than it can to the other. However, one can see how in the well nourished child both factors could operate together to the advantage of a wide shadow, whether it be thymic or nonthymic.

SUMMARY

1. The case of a patient, 17 months old, is presented who under the fluoroscope and in the roentgenogram shows a wide shadow in the thymic region which, according to present conception, is considered abnormal.

2. This shadow in its most marked form extends both to the right and to the left of the vertebral column, while in its mediumly severe form it projects out only to the right.

3. This wide shadow is sharp in outline and has a definite shape, similar to that of a miniature lung, with an angle at the lower, outer, right side which seemingly cannot be produced by the vena cava, nor by the auricle, as it extends clearly separated from the heart out into the lung area, and not toward the middle line, as would be the case if a distended auricle were responsible for it. No pulsations were ever seen in the shadow or any part of it, and until contradictory evidence is advanced the shadow is accepted as of thymic origin.

4. This abnormal shadow can be replaced by one of normal size if the patient takes a deep inspiration.

5. The abnormal shadow can be brought out in its most marked form by having the patient expire deeply and forcefully. Both observations can clearly be seen with the aid of a fluoroscope.

6. The diaphragm, as observed under the fluoroscope, rises with the development of the abnormal shadow and descends with the development of the normal.

7. Frequent exposures to the roentgen ray for a period of over five months have not changed the size of the thymus, nor have they influenced in a dependable manner the general condition of the patient. As a matter of fact, the patient has improved, while his thymic shadow has remained the same. The general improvement can well be explained by the dietetic changes instituted and the administration of atropin.

8. In producing the abnormal shadow in expiration the diaphragm seems to be the most important individual factor, either directly and mechanically by pushing the heart upward and so forcing the thymus in the same direction and also outward when ascending markedly or indirectly by increasing the intrathoracic pressure to a sufficient degree to move the thymus upward in a mechanical manner, or by retarding decidedly and in forced extreme expiration nearly entirely the venous outflow from the thymus, while still permitting its arterial inflow, and by so creating an acute engorgement and enlargement of the gland, which would cause the above factors to operate even more advantageously, and which would explain better than anything else the miniature lung-like development of the shadow under the fluoroscope.

9. In establishing the return to a normal picture the descent of the diaphragm would seem to operate by relieving the causative factors indicated above, and so allowing the thymus to descend down toward and over the middle of the heart and to empty itself rapidly following the suction effect of inspiration, especially when deep.

10. The wide shadows in their most marked form appeared on both sides, especially when viewed under the fluoroscope, but more on the right than on the left. In mediumly wide shadows only the right side was represented. Consequently, it is not justifiable to conclude that a picture showing a shadow limited to the right side comes from a patient who is unable to develop a shadow on the left side as well,

if given the proper conditions, nor can we conclude on the same basis that this shadow on the right side has nothing to do with the thymus gland and has been produced by some other factor such as an enlargement of the vena cava or auricle.

CONCLUSIONS

1. In order to have accurate knowledge as to the actual size of the thymus it is necessary to examine the gland under the fluoroscope and watch its position and condition at the various phases of respiration, especially in the development and at the end of a somewhat prolonged and forceful expiration, and again during a deep inspiration following the type of expiration just described.

2. If roentgenograms are made, an attempt should be made to get pictures both in deep inspiration and deep expiration. It may be well likewise to first attempt to get a picture while the child is breathing quietly and normally. It must, however, be realized that to procure roentgeograms of the thymus in the different respiratory phases is most difficult, uncertain and time consuming, and, therefore, it is suggested that the fluoroscope be always used to check the findings of the roentgenogram.

3. That unless the thymic shadow is observed as suggested above, a normal shadow obtained following a previous abnormal one does not mean an actual reduction in size of the gland.

4. The findings reported might explain the contradiction of reports according to which clinical improvement was obtained by exposure to the roentgen ray in cases where the thymic shadow was normal. It is possible that these cases really had an enlarged thymus, and that the picture just happened to have been taken during deep inspiration or very superficial expiration. It is, of course, also possible that in such cases the enlargement of the thymus is in the anteroposterior direction.

5. In all probability the position of the diaphragm directly and mediastinal or indirectly by influencing the intrathoracic pressure is more responsible than any other one factor for the difference observed in the pictures taken on the one hand in extreme inspiration and on the other at the end of a marked and forceful expiration.[11]

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11. The following references may also be consulted: von Reuss, A.: Die Krankheiten des Neugeborenen, 1914, p. 263; Friedlander, A.: Enlargement of the Thymus Treated by the Roentgen Ray, Tr. Am. Pediat. Soc. **29**:80, 81, 1917.

DISCUSSION

DR. LADD: I have been interested in several cases of undoubted enlargement of the thymus gland and in several cases suspected of being enlargement of the thymus gland that proved not to be. I have noticed the shadow in the plates, but I have not paid so much attention to the width as to the curves. The curve of the great vessels is almost always a straight line or slightly concave and the outline is much more distinct than the shadow of the thymus itself. The cases that we concluded were those of enlarged thymus showed a distinct convexity on the right, being more convex on the right than on the left side. I think the width of the shadow alone does not indicate enlargement of the thymus. If the shadow is enlarged both to the right and left and is convex in outline, one may reasonably diagnose enlarged thymus.

SIX CASES OF PYLORIC STENOSIS

H. M. McCLANAHAN, M.D.

OMAHA

Since June, 1919, I have had under my care and treatment six cases of congenital hypertrophic stenosis. All of these cases complied with the following syndrome of symptoms, namely, loss of weight, vomiting several times a day—frequently expulsive in character—stools small and dark without any evidence of milk digestion, visible peristaltic wave, and scanty urine. Movable tumor by palpation in three of the four cases recovering without operation. In one of the four cases not submitted to operation, the diagnosis was further confirmed by the roentgenogram. Four of the six patients recovered under gruel feeding. Their ages when they came under observation were 5, 5, 7 and 11 weeks respectively. These patients were placed on a thick gruel feeding in the manner described by Dr. Sauer and later by Dr. Langley Porter. The rate of gain varied, but all made a slow but steady improvement. After returning home I have had regular reports from all of them. Their ages and weight May 20 were as follows:

Baby G., 11 months; 18 pounds. Baby R., 9 months; 14½ pounds. Baby M., 5 months; 12½ pounds. Baby B., 7 months; 13¾ pounds.

The fifth case, Baby B., came under observation Jan. 2, 1920. This infant made fair progress for two weeks, but the parents seeing the result of an operation in the next case to be reported, demanded an operation. The patient was operated on by Dr. Jonas Feb. 2, 1920. He rallied slowly, and after twenty-four hours made a steady gain in weight. May 20 its weight was 16 pounds 12 ounces; age 6 months. As the parents of this infant live in Omaha, I have seen the child on frequent occasions. It is my belief that this infant would have recovered without operation.

The sixth case, Baby H., I wish to report more in detail.

REPORT OF CASE

Infant born Dec. 2, 1919. Birth weight, 10½ pounds. Breast fed for two weeks, when it began vomiting. Weaned at end of four weeks. Brought to the hospital January 1. Attempt made to establish breast feeding without success. Weight on admission, 7¾ pounds. Parents healthy. Continued on gruel feed-

ing from January 1 to January 24. During this period it lost 1 pound in weight. January 4, had a temperature of 104 F. Lungs and heart negative. January 9, exudate was observed on the tongue and cheek. Stain made from this culture revealed staphylococci. No mycelium. From January 20 to January 24 the vomiting was more persistent; and the vomited matter consisted chiefly of mucus with many blood streaks and occult blood on test. The morning of the twenty-fourth the temperature was 105 F., and for twenty-four hours there had been complete anuria. On this day the father implored us to have the infant operated on.

Operation at 3 p. m., performed by Drs. Kennedy and Henske. Infant was on the table seventeen minutes. The pyloric mass was simply incised and separated. At my suggestion 10 ounces of sterile physiologic sodium chlorid solution was instilled into the peritoneal cavity during the operation. Infant was placed in bed with hot water bottles. Five per cent. glucose solution was given by proctolysis. The infant rallied and was given water by mouth by the dropper for the first twenty-four hours. January 25, the temperature was 104.6 F.

On this day the patient was given the following formula:

Whey	1 ounce
Sterile water	1 ounce
Sodium citrate	1 grain

2 ounces every three hours.

It had one stool dark in color. The kidneys, however, acted freely. January 26 the temperature was normal. Emesis twice in twenty-four hours. After this date the stools were yellow in color and the kidneys continued to act freely. This formula was gradually strengthened by the addition of milk.

February 1 there was a profuse discharge from the left ear. Dr. Wohl (pathologist) reported that the pus showed the presence of staphylococci. From the date of the operation until March 20 the improvement was very slow, the weight varied from day to day, but on the latter date there was a gain of one pound. The infant returned home weighing 7¾ pounds.

Weekly reports from the baby after its return home showed a more rapid gain in weight. May 20, 1920, its age was 5½ months and weight 12 pounds. The parents reported in a letter that the infant was well and active, the stools normal, and that there was no vomiting.

At the operation the walls of the stomach were seen to be dark in color in striking contrast with that of the intestines.

In this case we were, therefore, dealing with an infant with congenital hypertrophic stenosis, a general staphylococcus infection, and undoubtedly an acute gastritis. This was the most critically ill infant I have ever seen placed on the operating table, and I have no doubt that the case would have terminated fatally without an operation.

A CASE OF PORTAL THROMBOSIS IN A CHILD THREE YEARS OF AGE

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BOSTON

Portal thrombosis is a rare condition and extremely rare in children. The following case is, therefore, of interest as recording the occurrence in a 3-year-old child.

REPORT OF CASE

M. R., 3 years old, was admitted to the Massachusetts General Hospital Dec. 22, 1919. Family and past history unimportant. Seven days before admission had an acute rise in temperature with a cough. The temperature on the third day was 106 F. The color was normal. That day the child passed a very dark stool of soft consistency. From that time until admission the child became increasingly pale and grew irritable and restless.

On the morning of admission a small ecchymotic area was noticed on the forehead and another over the sacrum. No more dark stools were seen. The physical examination on admission to the hospital showed a very pale girl, skin almost waxy, who seemed acutely ill. The areas of ecchymosis mentioned in the history were present, both about the size of a quarter of a dollar. There were no other ecchymotic areas and no petechiae. The heart measured 7.5 cm. to the left of the midsternum, 3 cm. beyond the nipple line and 2 cm. to the right of the midsternum. The point of maximum impulse was 5 cm. to the left of the midsternum, 2 cm. outside the nipple line in the fifth space. The character of the impulse was not abnormal. There was a loud systolic murmur heard all over the precordia. The first sound at the apex was loud. The second sounds were equal and not accentuated. The lungs showed no dulness, but a few moist râles were heard over the back, especially at the bases. The abdomen was not distended and no masses were felt. There was no ascites. The liver extended from the fifth rib to 2 cm. below the costal margin, where the edge was felt. The spleen was palpable just below the costal margin and was tender. The rectal examination was negative. The examination in other respects was normal. The urine was normal. The stools were normal. The guaiac test was negative.

The blood showed: hemoglobin, 40 per cent.; erythrocytes, 1,960,000; leukocytes, 18,000. Differential count: polymorphonuclears, 60 per cent.; small mononuclears, 24 per cent.; large mononuclears, 10 per cent.; transitional cells, 3 per cent.; neutrophilic myelocytes, 3 per cent. Three normoblasts; slight poikilocytosis; no polychromatophilia; blood platelets normal; reticulated reds, 6 per cent. Blood culture was negative. The Wassermann was negative. The von Pirquet and the intradermal tuberculin tests were negative. The blood pressure was, systolic 90 and diastolic 70. The roentgenogram of the chest showed an enlarged heart, otherwise not remarkable. The electrocardiagram showed sino-auricular tachycardia (rate 160), no auricular hypertrophy or ventricular preponderance. The temperature on admission was 102.8 F.; pulse, 160; respirations, 25.

She was transfused within a few days with only temporary benefit. The blood picture remained essentially the same, except for temporary modification throughout the course of the disease. The heart remained practically unchanged. The abdomen became gradually distended with fluid, the superficial veins in the upper portion became enlarged, the spleen increased greatly in size, finally reaching nearly to the umbilicus and assuming a transverse position in the abdomen so that it was somewhat doubtful whether it was a spleen, although the notch was easily felt. The temperature varied from 100 to 104 F., usually ranging about 101 F. in the early part of the disease and about 103 F. in the latter part of the disease. The pulse remained rapid throughout. The respirations were about 30 or 35, except at the end, when they rose to 45 or 50.

About six weeks after admission she vomited a large amount of bright red blood. She was transfused again, but died at the end of a week, practically two months from the onset of the infection.

Comment: The striking things about this patient were the persistent fever beginning abruptly and running a constant course until death, with evidence of some intra-abdominal condition which produced ascites, an enlarged liver and spleen, engorgement of the superficial abdominal veins, severe anemia and intestinal hemorrhage. In life we were not able definitely to make a satisfactory diagnosis.

Necropsy: At the necropsy there was found a thrombosis of the portal vein and its great radicles, passive congestion of the spleen, ascites, hypertrophy and dilatation of the heart, edema of the lungs and anemia.

Diagnosis: This was undoubtedly a thrombosis of infectious origin arising in connection with the initial infection of the respiratory tract.

The necropsy was done by Dr. Oscar Richardson. A complete protocol is appended.

Necropsy Report.—The dead body of a white girl, 3 years of age, 96½ cm. long, well developed, and poorly nourished.

Head: Not examined.

Trunk: The skin generally is very pale. In the region of the upper part of the right thigh, anterior aspect, there is a linear wound 3½ cm. long, in stage of healing.

Abdomen: Distended from side to side.

Umbilicus: Pouts slightly.

Cutaneous Veins: Rather prominent. On section, subcutaneous fat very small in amount. Muscles, pale.

Appendix: Negative.

Peritoneum: In the region of each flank it shows much injection of the vessels. The peritoneum otherwise is negative.

Esophagus: Negative. The mucosa is pale.

Stomach: On section shows a very pale mucosa, but otherwise it is negative. Pylorus, negative.

Intestines: The walls and mucosa are very pale; otherwise they are negative.

Mesenteric and Retroperitoneal Glands: Negative. The anterior margin of the right lobe of the liver is three fingers breadth below the costal border, in the right mammillary line.

Diaphragm: Right, fifth rib; left, fifth interspace.

Pleural Cavities: Contain a small amount of thin, pale, clear fluid.

Pleural Adhesions: None.

Thymus Gland: There is but little if any gland tissue remaining.

Trachea and Bronchi: Contain much thin, pale, clear fluid. The mucosa is pale.

Bronchial Glands: Negative.

Lungs: Present no areas of consolidation. The pleura is smooth and shining. The tissue is pale to pale reddish and yields a large amount of thin, finely frothy, pale to pale reddish fluid.

Pericardium: Negative.

Heart: Enlarged: Weighs 100 gm. Myocardium is of good consistence, pale. Right ventricle wall measures 2 mm.; left ventricle wall, 6 mm.

Columnae Carneae: Fairly well marked.

Cavities: Left, considerable dilatation. Right, slight dilatation. The valves are negative.

Coronaries: Negative. Foramen ovale, closed.

Aorta and Great Branches: Negative.

Pulmonary Artery and Veins: Negative.

Venae Cavae and Great Radicles: Negative. The portal vein, from the region of its entrance into the liver, down along its entire course, together with its great radicles, shows thrombotic occlusion. The thrombotic plugs consist of grayish-yellow granular material, distinctly adherent in places, with prolongation into plugs, brownish-red to blackish-red, firmer and softer, with more or less adhesion. The condition extends to the region of the mesenteric insertion, along the small intestine and the first portion of the large intestine.

Liver: Weighs 470 gm. The tissue is of good consistency, very pale.

Gall-bladder Wall: Edematous. The mucosa is negative.

Bile Ducts: Negative.

Pancreas and Duct of Wirsung: Negative.

Spleen: Weighs 165 gm. Considerably enlarged. The surface is smooth. The tissue is of increased consistence, somewhat leathery, pale gray-red.

Suprarenals: Negative.

Kidneys: Large. Combined weight, 145 gm. The capsules strip, leaving smooth, very pale surfaces. On section the markings are made out, the cortex is 4 mm., and the section surfaces are very pale. The tissue is rather wet.

Pelves, Ureters, Bladder, Uterus and Adnexa: Negative.

Microscopic Examination.—

Kidney: Negative.

Veins: Two sections show thrombi partially organized.

Liver: Negative.

Spleen: Interstitial tissue seems increased in amount.

DISCUSSION

DR. ABT: Did the child have a chill and was there any ear involvement?

DR. SMITH: With reference to the organisms, we were not able to identify any organism. We had no chance to make cultures, since we were not able to obtain a satisfactory specimen. This child did not have ear infection and did not have a chill.

A CASE OF CARDIOSPASM

GODFREY R. PISEK, M.D.

NEW YORK

It is only within comparatively recent years that instances of spasm of the cardia, among adults, have been reported in any number, while the occurrence of this condition in early life is sufficiently unusual to justify the report of a case. The pediatrician may well consider these cases worthy of study, for the reason that symptoms in adults may be traced to defects, or to an origin in early life.

Méry,[1] Beck,[2] Morgan[3] and Adams,[4] La Fétra[5] and Graham[6] have reported cases of cardiospasm—most of these on analysis proved to be conditions having an anatomic basis.

Neurotic or primary cardiospasm is attributed by some authorities to a contraction of the left crux of the diaphragm, by others to defective innervation or to localized atony of the esophagus. That the condition does not respond to treatment as readily as one would be led to suppose by the literature is shown by the following case:

REPORT OF CASE

E. P., female, aged 12 years, first came under observation in September, 1919.

Family History.—Good. Father is physician. Other children are well and strong.

Past History.—Normal delivery, at term, with a birth weight of 10 pounds. Regarded as a perfectly healthy infant and child. At the age of 3 or 4 years, she "developed a strong will," and is said to have been "temperamental." This "wilfulness" grew stronger, so that at the age of 10 she would become "highly excitable" if crossed. She was, otherwise, an outdoor, athletic child, but with a "peculiar appetite" in that she disliked vegetables, eggs and sweets.

Present Condition.—About one month ago she suddenly said, "The food chokes me," and left the table to vomit. Since that time, at every meal, her food seems to choke her and feels as though it would not go down. This occurrence is independent of whether the food is relished or not. At night, also, a similar difficulty comes on which she describes as "sort of strangles me."

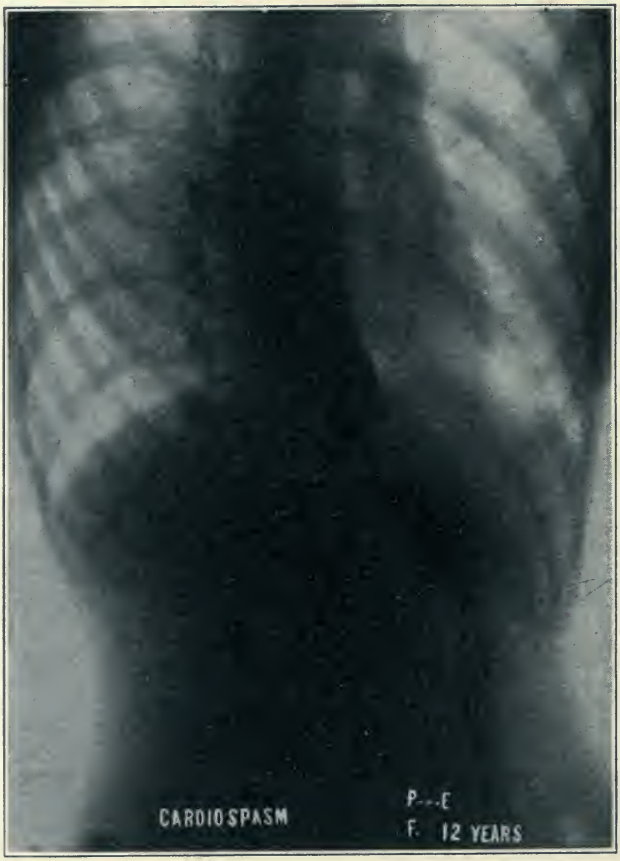
Further questioning elicited the fact that for the past year, food, either liquid or solid, would occasionally "stick in her throat," but by "thumping her chest" she would be able to swallow it.

A cough developed in connection with the night spasms, unconscious so far as the patient was concerned, but very noticeable to the family. Her father never found any physical signs to account for this symptom, and even codein gave no relief.

Physical Examination.—Overgrown girl, with long, narrow thorax, and with good bony development. Musculature better in upper than in lower extremities.

Mentality: Normal. Special senses, normal.

Thorax: Some retraction of supraclavicular and infraclavicular spaces. Thyroid: Not enlarged. Heart: Negative. Pulse: Regular; good quality. Blood pressure: Systolic, 85; diastolic, 58. Lungs: Negative. D'Espine's sign: Negative.



Abdomen: Negative.

Nervous System: Reflexes normal. Coordination fairly good. Slight tremor of upper eyelids. Slow response to relaxation test.

Posture: Tendency to relaxation of spine and bowing of shoulders. No curvature. Scapulae prominent. Weight: 100½ pounds. Height: 66¼ inches. (Weight in proportion to her height should be about 119 pounds.)

Laboratory Examinations.—

Urinary Findings: Evidence of orthostatic albuminuria.

Fluoroscopic and Roentgenoscopic: Confirmed the diagnosis of cardiospasm, made on history and negative physical findings. (Dr. L. T. LeWald.)

Esophagoscopy: Examination under general anesthesia failed to demonstrate an anatomical basis. Moderate dilatation accomplished at the same time. (Dr. N. W. Green.)

Treatment.—After the initial dilatation, bougies were passed at about fortnightly intervals, until her departure for Florida in March, 1920. This change was decided on because she did not prosper physically, in spite of atropin treatment, dilatation, segregation and a carefully supervised dietary. Her symptoms had improved materially, but there had been a loss of 7 pounds of weight, to 93 pounds. The hemoglobin at this time registered 75 per cent.

In the South she did well at first, even attending a private school and appearing to enjoy life. Then she contracted malaria, for which she received appropriate quinin treatment. She lost weight quite rapidly, going down to 80 pounds—more than twenty pounds below her former standard. Her original symptoms referrable to cardiospasm returned.

On returning North, a further attempt to exclude a tuberculous focus was made by repeated physical examinations, the roentgen ray, the von Pirquet and examination of the sputum. All these tests were negative. Examination of the gastric activity showed the secretion and the motility to be well within the normal limits.

A second fluoroscopy and roentgenoscopy showed a "considerable dilatation of the esophagus with a smooth fusiform constriction at the cardia." (Dr. W. H. Meyer.)

The patient is under observation at the Postgraduate Hospital, New York. Bougies are being passed about every fourth day. The diet consists of bland food, measured to contain from 3,000 to 3,500 calories per day, while her only medication is atropin in small doses. There has been a gain of fifteen pounds in weight—to 95 pounds—in the past twenty-nine days.

Whether it will be considered necessary to pass a duodenal tube, thereby giving the stomach a complete rest for a term, is still a question, but as the patient is doing so well at present, it is considered best to let well enough alone.

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4. Adams, S. S.: Tr. Am. Pediat. Soc., 1908.
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DISCUSSION

DR. GRIFFITH: In connection with a series of neurotic and psychasthenic manifestations in children, which I reported some years ago, there was one in a boy of 10 years, suffering from spasm of the esophagus. I cannot say whether or not it was cardiospasm, as roentgen-ray pictures were not taken as frequently then as now. He could swallow liquid, but had apparently an inability to ingest solid food. He was referred to a very able surgeon who felt convinced that the condition was one of organic stenosis of the esophagus.

There were certain features which led me to believe that it was not of this nature, and when the boy was etherized for operation it was found that any proper sized bougie could be passed without the slightest difficulty. The condition was clearly hysterical, and was cured by sending the child from home to a boarding-school.

DR. PISEK: I do not think one is justified in trying to pass a bougie without a preliminary esophagoscopy. The neurotic element is not always of the kind so easily dealt with as in the case Dr. Griffith has cited, and dilatation alone is not always effective in the cure.

PRIMARY SARCOMA OF THE THYMUS

L. EMMETT HOLT, M.D.

NEW YORK

REPORT OF CASE

A female child, 6 months old, was admitted to the Babies' Hospital March 18, 1920, on account of a severe anemia. Pallor had been noticed for only three or four weeks, but had increased steadily and rather rapidly during that time. Though no temperature record had been taken, the mother thought her feverish at times. For two weeks small hemorrhagic spots had been coming out on the abdomen, chest, extremities and neck; latterly they were not so abundant nor so large in size. No hemorrhages from any of the mucous membranes; no dyspnea or convulsions. Few other symptoms had been present; the appetite remained good; there had been a moderate loss in weight; the bowels were constipated; she had vomited but once since the onset.

The child was small at birth; had been breast fed up to time of admission; had gained slowly and had had no previous illness. The family history was excellent; the parents were both healthy, as were two other children; none dead; no miscarriages.

Physical Examination.—On examination, there was found a delicate looking infant, extremely pale, the face, neck, trunk and extremities showing many small petechiae, the largest being only 2 or 3 mm. in size. The blood examination showed marked secondary anemia only; hemoglobin, 40 per cent.; erythrocytes, 1,600,000; leukocytes, 5,000; polymorphonuclears, 73 per cent.; lymphocytes, 27 per cent.; nothing else of importance. A systolic murmur was heard at the base of the heart. No signs of disease in the lungs; spleen enlarged, felt about 2 cm. below costal margin. A general but not marked glandular enlargement noted in cervical, postauricular, axillary and inguinal regions.

The infant lived for four days after admission; the temperature was constantly elevated, ranging from 99.5 to 103 F. Râles appeared at the bases of both lungs, but there were no signs of consolidation.

Treatment.—A transfusion was done on the second day; 150 c.c. of blood from the mother was injected into the superior longitudinal sinus. After this the symptoms were distinctly worse. The hemoglobin fell to 25 per cent.; the erythrocytes to 800,000; leukocytes, 4,000; polymorphonuclears, 64 per cent.; lymphocytes, 36 per cent. The child grew progressively weaker in spite of stimulation and died apparently of exhaustion.

Diagnosis.—The case was regarded as one of severe secondary anemia, cause unknown.

A necropsy ten hours after death by Dr. Martha Wollstein: There are minute purpuric spots over the entire body, except the palms and soles. They are least numerous on the face. About 20 c.c. of serous fluid, straw colored, is present in the pleural cavities.

Thymus: The thymus weighs 36 gm. It measures 6 by 8 cm. and covers the entire pericardial sac, extending downward to the level of the heart apex and upward to the lower border of the larynx. There are pin-point hemorrhages

beneath its capsule. The substance of the thymus is very firm and nodular. On section, it shows yellowish lines outlining red areas, giving the appearance of a thickened septa of interstitial tissue with congestion and hemorrhage into the gland substance. There are areas in some of the lobules which have the white, smooth, glistening appearance of sarcoma.

Lymph Nodes: The adjacent lymph nodes are slightly hyperplastic. None are larger than ½ cm. in diameter. They are red on section and show no metastases. On the right side of the trachea one mediastinal node is necrotic, but not tuberculous. A bronchial lymph node on the right side, ½ cm. in diameter, contains a reddish nodule which looks possibly metastatic in character.

Lungs: Minute subpleural hemorrhages are present over all the lobes of both lungs. The pleura is adherent to the outer surface of the pericardium on the left side, and over the right upper lobe. There is recent bronchopneumonia in the posterior half of both the upper and lower lobes of the right lung. In the left lung there is a smaller area of bronchopneumonia in the upper and lower lobes. In the left lower lobe the consolidated area, on section, is greyish white, smooth and suggests new growth rather than old pneumonia. The right middle lobe is aerated throughout. Considerable emphysema is present. No circumscribed nodules are visible or palpable in the lung substance.

Heart: The heart is normal in size. On the ascending portion of the arch of the aorta there is a raised grey nodule, 2 mm. in diameter, with a slightly hemorrhagic base, apparently a metastasis. The outer surface of the heart is grey in color due to a decided thickening of the visceral pericardium. There are many capillary hemorrhages beneath it. The myocardium and all the valves are normal. The endocardium lining the auricles is thickened, grey and wrinkled. The foramen ovale is closed.

The pericardial sac contains clear, yellow serum somewhat increased in amount. The inner surface is glistening and normal. The parietal pericardium is decidedly grey and thickened.

Spleen: The spleen weighs 60 gm.; it measures 6 by 8 cm. The substance is very firm. The splenic pulp is mottled, dark blue in color, with pale, red nodules which are not necrotic. The largest is 3 mm. in diameter. The splenic capsule is irregularly thickened and its surface roughened; three small nodules similar to those in the pulp are visible on the spleen surface.

Liver: The liver is normal in size; its substance very firm. The capsule near the suspensory ligament is thickened. On section the liver substance shows many areas of parenchymatous degeneration. It is slightly fatty, but no metastases are seen.

Other Organs: The kidneys, bladder, suprarenals, uterus, ovaries, tubes, pancreas and stomach are all normal.

The duodenum and jejunum are normal. The Peyer's patches in the ileum are slightly hyperplastic. The solitary follicles of the colon are visible; some are outlined by narrow hemorrhagic zones. No ulcers are present. The rectum is normal.

Abdominal lymph nodes are slightly enlarged and hemorrhagic in color. The largest measures 1 cm. in length.

Anatomic Diagnosis.—Thyoma, with metastases in lungs, bronchial lymph nodes and spleen; bronchopneumonia with fibrous pleurisy; hyperplasia of spleen and lymph nodes; chronic perisplenitis and perihepatitis; parenchymatous and fatty degeneration of liver; subserous and subcutaneous petechial hemorrhages.

Bacteriologic Examination.—Staphylococcus aureus in pure culture grew from the fluid in the peritoneal and pericardial cavities.

Microscopic Examination.—Thymus Gland: Fibrous connective tissue carrying blood vessels form an indefinite outline for lobules which are filled with polyhedral cells having an acidophile cytoplasm. Many of their nuclei show mitotic figures. Giant cells are more numerous in some lobules than in others, and vary both in size and in the number of their vesicular nuclei. Small round cells of the lymphocyte type are not numerous. They are present chiefly at the periphery of the lobules, the center of which contains small necrotic areas in many instances. Blood vessels are numerous but small. No well-formed Hassall's corpuscles are present. The growth is a thymoma of the sarcomatous, not carcinomatous type.

Spleen: There are several collections of polyhedral cells similar to those in the thymic neoplasm but without giant cells. The blood vessels in the pulp are very much congested and the connective tissue is thickened.

Lymph Nodes: Several small lymph nodules are completely replaced by collections of tumor cells, leaving only narrow strands of lymphoid cells. Giant cells are numerous and small necrotic areas are present in the nodules.

Left Lung: The sections show bronchopneumonia with much intraalveolar hemorrhage. There is an area of irregular outline in which alveolar structure is lost, and which is made up of polyhedral cells like those in the neoplasm. One giant cell is seen. This metastasis shades gradually without encapsulation into the surrounding pneumonic lung.

Microscopic Diagnosis.—Thyoma (sarcoma) with metastatic deposits in lungs, spleen and bronchial lymph node.

HEART DISPLACEMENT APPARENTLY DUE TO MEDIASTINAL EMPHYSEMA FOLLOWING ASPIRATION PNEUMONIA *

E. C. FLEISCHNER

SAN FRANCISCO

Heart displacement in children is ordinarily due to the presence either of free fluid or free air in the pleural cavity. The following case illustrates a marked type of displacement of the heart to the right in which neither pleuritic effusion, hydrothorax nor pneumothorax played a rôle.

REPORT OF CASE

G. P., aged 4 years, Sept. 10, 1919, at 4 p. m., fell into a pile of sand, and on being picked up by his mother stated that he had swallowed some of the sand. No effect was evident at that time, but when the boy was put to bed at 6 p. m., two hours after the accident, musical sounds were heard all over his chest, and he was breathing very rapidly.

He was taken to the Children's Hospital four hours after the accident, at which time physical examination revealed nothing beyond the presence of a large number of sibilant and sonorous râles over both lungs anteriorly and posteriorly. Roentgen-ray examination made one day after the accident was negative (Figure 1). Temperature and pulse were practically normal for about forty-eight hours. Five days after the aspiration of the sand, there were definite signs of bronchopneumonia on the left side, particularly over the middle lobe. Eight days after the accident, physical examination disclosed that the heart was very markedly displaced to the right. Roentgen-ray examination at that time showed a profuse bronchopneumonia of the left lung and the heart very markedly pushed to the right side (Figure 2). The explanation of this displacement was not apparent for six days. September 24, subcutaneous emphysema developed suddenly in the supraclavicular space on the right side, extending upward, backward and downward over the right lung posteriorly as far as the pelvis. On account of the very serious general condition of the child, roentgenogram was not taken at that time. The air under the skin was gradually absorbed. At the end of one week it was no longer apparent.

October 7, about two months after the accident, roentgen-ray examination revealed (Figure 3) the heart still markedly displaced to the right with a diffuse pneumonic process of the left lung, which at this time involved the lower lobe more than on previous examination. The patient continued to have a septic temperature; he coughed a great deal, and on physical examination, besides the heart displacement, showed diminished breathing all over the left

* From the Department of Pediatrics of the University of California Medical School.

Figure 1

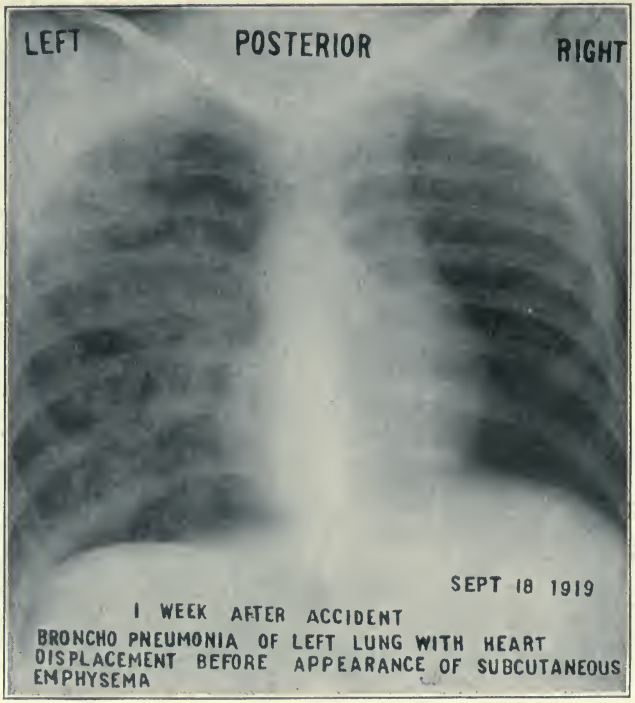

Figure 2

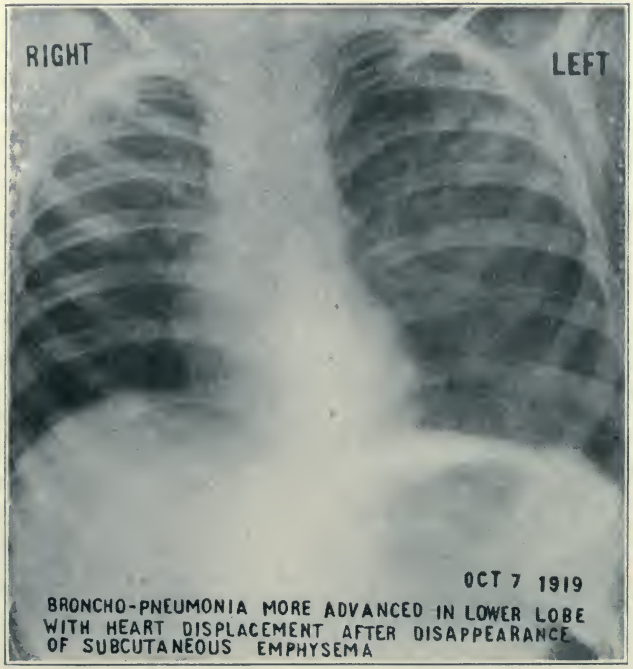

Figure 3

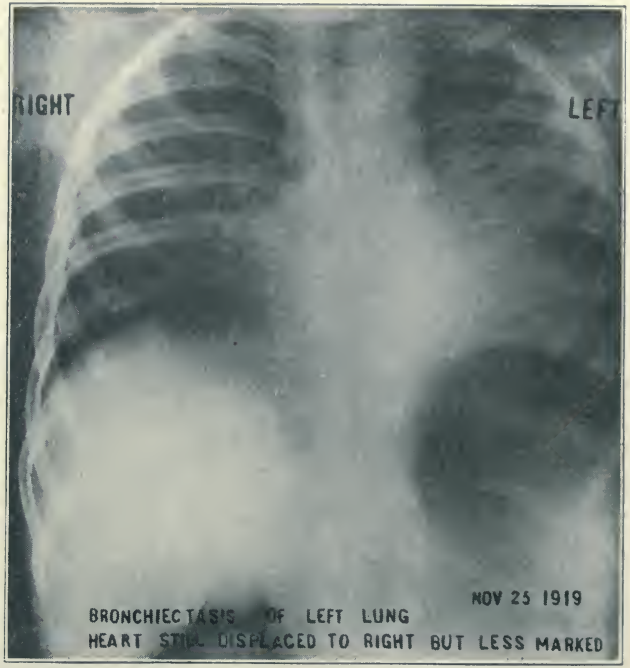

Figure 4

Figure 5

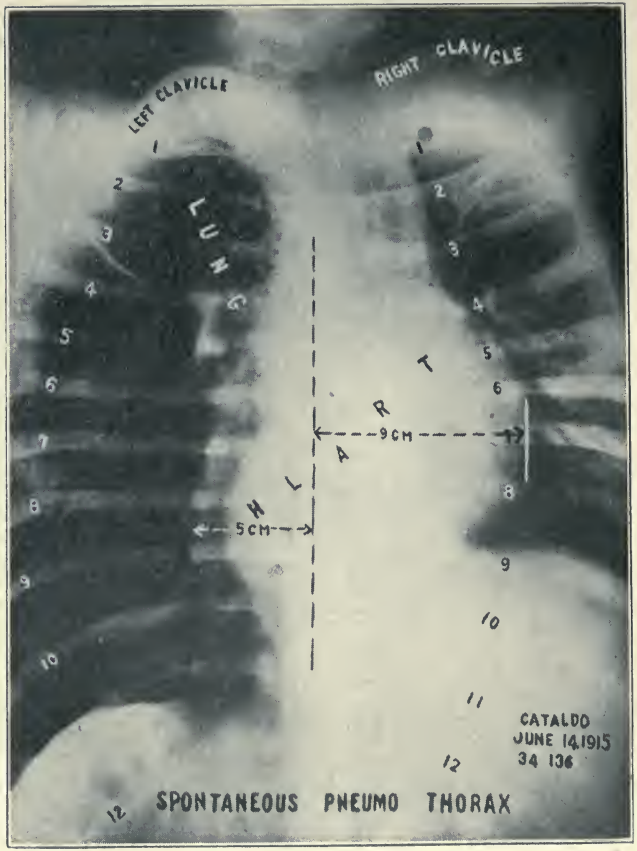

Figure 6

lung, bronchovesicular in character, with a variety of adventitious sounds. He was returned to his home. His temperature became very much more septic in character; he emaciated more rapidly and expectorated large quantities of purulent sputum. Bronchiectasis was suspected. He was taken back to the hospital, a fourth roentgenogram (Figure 4) was taken which showed a diffuse bronchopneumonia still present with small bronchiectatic cavities.

The child was then taken to the country and was not seen for several months. His temperature gardually reached normal, his cough diminished, the amount of sputum grew progressively less; he gained weight and was brought back March 19, 1920, about six months after the original accident. Physical examination was negative and the last roentgenogram (Figure 5) taken at that time showed an apparently normal chest.

COMMENT

The case is essentially interesting on account of the marked displacement of the heart which was apparently due to the rupture of some of the air vesicles of the inflamed lung allowing free air to escape into the mediastinum, from which it made its way up under the right clavicle and posteriorly over the right side. Were it not for the fact that subcutaneous emphysema manifested itself, it would have been very difficult to have excluded an intense interstitial emphysema of the left lung as the cause of the displacement, but considering the fact that the air escaped from the inflamed lung and not having been able to prove its presence in the pleural cavity, one is forced to the conclusion that the heart could only have been displaced by the presence of air in fairly large quantities in the mediastinum.

A careful review of the literature fails to disclose any record of a similar observation.

DISCUSSION

DR. SMITH: I should like to record a case in which there was cardiac displacement associated with atelectasis of the upper lobe of the lung. This child had the heart displaced to the left and in the transverse position. The whole upper right chest was dull to percussion. At autopsy there was emphysema of the upper left lobe of the lung so that it filled nearly the entire right chest and the upper part of the left. The rest of the lungs were compressed.

DR. FLEISCHNER: The roentgenograms of the lungs in this case suggested that there was a certain amount of interstitial emphysema on the left side, but unfortunately there was no postmortem so we cannot say just what occurred.

THE DUCT SIGN IN MUMPS*

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ANN ARBOR, MICH.

An epidemic of mumps among the students of the university during the academic year 1914-1915 gave us an unusual opportunity to watch from day to day quite a number of patients sent to the contagious hospital for treatment. Mumps is a disease which is usually seen but once by the attending physician and, very commonly, the diagnosis is made by some member of the family at the time of an epidemic. This may explain why the sign I wish to describe has not attracted general attention. The difficulties in the differential diagnosis of mumps are so slight that it would seem hardly necessary to describe a new sign or one which may have been fully recognized before, but which, as seen by us, has not found its way into the textbooks. There are, however, times when swellings on the cheeks not due to specific parotitis offer some difficulties in diagnosis. The duct sign may prove to be of considerable value in settling the question.[1]

It is a routine practice on my service at the contagious hospital to examine for enanthems as carefully as for exanthems, and to record the findings whether positive or negative, and to note any peculiarities. My attention was called to a red spot on the buccal mucous membrane at the opening of Steno's duct in a case of mumps which entered the hospital Nov. 28, 1914. I did not recall ever having observed any change in the ducts in mumps before this time, and decided to watch for its occurrence in other cases. Since that time, notes have been made on fifty-seven hospital cases, a sufficient number—if the sign has any constancy—to establish it as characteristic of the disease. It is not surprising that this sign has been quite

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1. Several authors refer to swelling of the mucous membrane at the opening of Steno's duct; Carr: Practice of Pediatrics, 1906; Cotton: Medical Diseases of Infancy and Childhood, 1906; Rochford: Diseases of Children, 1912; Feer: Lehrbuch der Kinderheilkunde, 1914.

Doubtless many have observed this duct involvement and have utilized it as a diagnostic point, but for some reason its significance has been considered so slight that the very large majority of standard texts make no mention of it.

generally overlooked because the spot is so small, is often hidden by the teeth and is usually single. If seen, it would, probably, not excite much attention because of its size. Frequent mention is made of the mouth cavity in mumps in the texts, but it is usually described as being negative.

DESCRIPTION OF THE DUCT SIGN

In a case of mumps, if the buccal mucous membrane is well separated from the teeth with a spoon handle and viewed in a good light, the orifice of Steno's duct on the affected side or sides will present a reddened spot measuring from 1 to 2 mm. in diameter. The duct will usually be found to project beyond the surface of the mucous membrane from 1 to 3 mm. In other words, the duct becomes teatulated. The duct is edematous and is usually pale, as a whole, thus accentuating the red central spot which, at times, gives the appearance of a minute ring because of the central opening which may appear darker. In some cases the greater part of the teating is slightly injected. Minute hemorrhagic points may be seen [2] scattered over an area surrounding the duct as great as 2 cm. in diameter. The orifice of the duct is tumefied and from it, at times, may be seen to exude a limpid fluid.

The involvement of the duct is a progressive and retrogressive change. The spot usually appears first and is followed by teatulation with retrogression in the reverse order.

The Red Spot.—The redness varies in shade from a faint pink to a deep inflammatory red; in many cases it never progresses to the deep red stage. As the swelling of the parotid gland recedes, the spot becomes paler and finally disappears. The spot develops early in the disease and, in all probability, precedes in most cases the observable swelling of the parotid gland, as witnessed by the presence of the spot on the unaffected side before the parotid swelling on that side appears (Case 8 [3933]).

The opening of Steno's duct, normally, is more marked in some persons than in others. The slight increased depth of color in such individuals is definitely not inflammatory and is easily differentiated after the duct sign is once seen. In a series of sixty-eight normal

2. Case 7 (1836) herein described. In one case yellowish spots were observed, Case 2 (1734).

persons, children and adults, the duct opening showed a faint but distinct pink color, differentiating it from the surrounding tissues in 14 per cent. of the cases.

The Teatulation.—Under normal conditions, at times, Steno's duct projects beyond the buccal mucous membrane. The opening of the duct, however, is not inflamed and in mumps when such a duct is present, if it is watched closely, it will be seen to undergo a definite change throughout the course of the disease. Teatulation does not always occur. In Cases 9 (4702) and 10 (4733) only the red spot was seen. A careful examination of the ducts in a series of sixty-eight normal persons, children and adults, one or both the ducts projected beyond the mucous membrane in 37 per cent.

The Duct Pallor.—The duct is usually pale, the pallor so well known in the ordinary mucous membrane swelling of the mouth. At times, this pallor gives the impression of a pale bluish areola surrounding the central red spot.

Duct Congestion or Injection.—This is described in Case 1836. In this case distinct hemorrhages were seen and seemed to be a part of the progressive change. Small hemorrhagic spots on the buccal mucous membrane are not uncommonly seen in children from traumatism—biting the cheeks—and it is possible that this patient may have bitten the projecting mucous membrane. The duct on this side projected fully 3 mm. and the ducts on both sides could be seen to run in between the upper teeth when the cheeks lay against them.

REPORT OF CASES

CASE 1 (1550).—Nov. 28, 1914. Male student, aged 22; second day of disease. The patient walked into the hospital. At this time he had swelling and tenderness in both parotid regions. The salivary opening on the left cheek was reddened. Patient had a temperature of 102 F. Later, the temperature reached 104 F. and he had pain in the pelvis which was referred to the testicle next day. No further observations were made in this case.

CASE 2 (1734).—March 10, 1915. Student, aged 20; first day of disease. Slight pain at the angle of the right jaw. There was no enlargement of the parotid, but there was slight tenderness on pressure over the angle of the right jaw.

March 11, The left parotid is only slightly reddened. The duct projects 3 mm. The right duct is not red nor does it project; it is flat. The left parotid is distinctly swollen. Patient was discharged on fourth day as a one-sided case of mumps.

March 18. Patient returns. The left duct is now red at the orifice and projects 3 mm. above the surface of the buccal mucous membrane. There is some edema of the duct and surrounding mucous membrane. About the duct on the right side are numerous miliary yellow spots.

March 19. The left parotid is distinctly swollen. Submaxillary glands not involved. Both papillae bulge 2 mm. Only slight redness of duct opening present. The little spots around the right duct are still present.

March 24. Left duct shows swelling, but practically no redness. Highest temperature, 102 F.

CASE 3 (1735).—March 10, 1915. Student, male, aged 22; second day of disease. Left parotid much swollen and tender. Right negative. Papillae of both ducts swollen and reddened.

March 11. Both ducts are reddened, particularly the right, and both project 1 mm. above the surface of the mucous membrane. The left opening is faintly seen and slightly dilated. The parotid on the right side is distinctly enlarged, the left only slightly.

March 17. Swelling of both parotid regions has about returned to normal. The opening of Steno's ducts still show slight swelling (tumefaction) more marked on the right. The papillae show a little redness.

March 18. The left duct projects slightly. The center is purplish and very edematous. The anemia around the duct measures 1 cm. in diameter, giving an edematous appearance. On the opposite side the redness has disappeared and the entire buccal mucous membrane appears swollen. The external swelling has almost entirely disappeared on the right side. It is still present on the left side.

March 19. There are dark purplish spots at the center of the duct opening on both sides. The left duct is flat; the right still projects and shows slight edema.

CASE 4 (1743).—March 15, 1915. Student, aged 22; second day of disease. Complained of continual aching in right parotid region. Right parotid swollen and tender. Right duct swollen with pinpoint redness at orifice of both ducts. Submaxillaries negative.

March 19. Duct on right side projects an area of 6 mm. in diameter. This area is edematous and has a bluish cast. There is an edematous center seen on the left side but it is not so marked.

March 29. Swelling at duct orifices almost gone, practically no redness. Highest temperature 104 F. Discharged fourteenth day.

CASE 5 (1823).—April 30, 1915. Male, aged 19; second day of disease. Examination showed a well developed case of mumps, right parotid. Both papillae were enlarged

May 2. Left parotid swollen. Duct projects. There are three pinpoint openings pointing outward, each showing a distinct reddening. The right duct shows no reddening, it is only swollen. Highest temperature 100 F.

CASE 6 (1834).—May 8, 1915. Patient, a nurse, second day of disease, entered contagious service with marked swelling and tenderness of the left parotid and a suggestion of swelling in right. There is no submaxillary swelling. The left duct shows a round bulging which projects from 1.5 to 2 mm. beyond the surrounding mucous membrane. The projection itself is not injected. In the center at the duct opening there is a small reddened depression. The right duct shows a similar picture.

May 11. Both cheeks are now characteristically swollen. The duct of the right side projects about 2 mm. At the center of the duct opening there is a

circumscribed deep red point The buccal mucous membrane is edematous, particularly in the space beyond the center of the duct. The red spot at the opening of the duct on the left side, the first involved, is becoming paler.

May 13. Submaxillary glands are now swollen. The patient has been having severe headaches for the past two days. No note on ducts.

May 19. There is still slight swelling of the left parotid. The right duct is negative. The left duct is still slightly elongated. The center is dull red.

May 20. The redness has disappeared and there is no evidence of congestion in the duct region.

Final Note. In this case, what commenced as a mild attack of mumps became complicated on the fourth day with severe headache which was not relieved by medicine and persisted for three days. The temperature reached 102 F. The patient complained of abdominal pain during this time, but we were unable to attribute it to ovarian or pancreatic involvement.

CASE 7 (1836).—May 11, 1915. Young woman, aged 20. Two days ago complained of soreness and swelling of right side of face. Yesterday both sides were swollen. This morning the right side shows only slight swelling. The left is characteristic. The right duct is very red at the center, an area of 2 mm. in diameter. There is slight projection or teating of the duct. The left duct projects further, fully 3 mm. The opening is very red and circumscribed about the orifice. Scattered over an area 2 cm. in diameter there are numerous small pointed red spots (hemorrhages) where the buccal mucous membranes are allowed to come against the teeth. The duct runs in between the teeth like a teat about 1 cm. in length.

May 13. Submaxillaries now involved.

May 17. Parotid and submaxillary swellings almost gone. Slight pigmentation of the ducts present.

May 19. Right duct negative. Left is still elongated; there is a dull red spot at the orifice.

May 22. No injection of orifices of ducts or surrounding mucous membranes.

CASE 8 (2159).—Dec. 15, 1915. Nurse, aged 23; second day of disease. Examination showed slight swelling of left side of face. Duct slightly enlarged but not red. Next day right parotid swelled.

December 17. Right duct not enlarged or reddened. Left duct projects, orifice slightly red. Highest temperature 103.8 F.

CASE 8 (3933).—Jan. 11, 1918. Male student, aged 19; second day of disease. Left parotid swelling marked, tender. There is no swelling of the right side of the face. The left duct is very edematous and inflamed, red. The right duct is only slightly enlarged, pink orifice.

January 22. Since last note the right parotid and duct have been characteristically involved. The swelling on the right side is disappearing while that on the left continues to be smaller and the left duct to be smaller and its orifice red. The right duct is normal.

January 24. Both ducts are normal. Highest temperature in this case, 102.2 F.

CASE 9 (4702).—May 7, 1919. A. M., female, aged 26. Patient presents herself at the clinic four hours after she first observed any symptoms, slight swelling of right face. She recalls that at bedtime there was a little soreness in her left cheek. Examination showed the right duct enlarged, projecting and red and the right parotid slightly swollen. Later on the left was involved.

CASE 10 (4733).—May 29, 1919. Young woman, aged 23. Two hours after she first noticed soreness and swelling in right jaw. There was difficulty in

The fifty-seven cases are here briefly tabulated.

ANALYSIS OF CLINICAL HISTORY OF FIFTY-SEVEN CASES OF MUMPS

Case Number	Date	Age	Sex†	Day of Disease First Seen	Teatulation of Duct		Reddening of Orifice		Highest Temperature
					Right	Left	Right	Left	
1550*	11/28/14	22	♂	2	—	—	—	+	102.0
1618	1/17/15	20	♂	2	+	0	+	0	102.0
1683	1/25/15	18	♂	3	+	—	+	—	100.8
1653	2/ 3/15	18	♂	2	+	+	+	+	103.0
1654*	2/ 3/15	20	♂	3	0	+	0	+	104.2
1662	2/ 6/15	18	♂	2	+	+	+	+	99.8
1660	2/ 8/15	22	♂	1	+	0	+	0	99.0
1701	2/24/15	22	♂	1	+	+	+	+	99.0
1697	2/22/15	22	♂	1	+	0	+	0	104.4
1700	2/22/15	23	♂	1	+	+	+	+	101.0
1711	3/ 1/15	18	♂	2	+	0	+	0	98.6
1735*	3/10/15	22	♂	2	+	+	+	+	100.8
1734*	3/10/15	20	♂	1	+	+	+	+	101.6
1743*	3/15/15	22	♂	1	+	+	+	+	103.4
1747	3/16/15	21	♂	2	+	+	+	+	99.0
1765	3/20/15	24	♂	—	0	+	0	+	101.0
1794[1]	4/11/15	23	♂	2	+	+	+	+	102.4
1823*	4/30/15	19	♂	2	+	+	0	+	100.0
1834*	5/ 8/15	21	♂	2	+	+	+	+	102.0
1836*	5/11/15	28	♂	2	+	+	+	+	98.6
1889	6/10/15	5	♂	2	+	+	+	+	Out-patient
2159*	12/17/15	23	♀	2	+	+	+	+	103.8
2421	4/11/16	18	♀	2	+	+	+	+	103.0
3898	12/12/17	21	♂	2	+	+	+	+	104.0
3910	12/14/17	23	♂	12	+	+	+	+	101.8
3933*	1/11/18	19	♂	2	+	+	+	+	102.0
4020	3/18/18	19	♂	2	0	+	0	+	98.6
3989	2/23/18	21	♂	4	0	+	0	+	99.0
3961	2/28/18	21	♂	2	+	+	+	+	99.0
4066*	4/17/18	21	♂	8	+	+	+	+	101.2
3998[2]	5/ 3/18	23	♂	7	0	+	0	+	104.0
4107	5/26/18	Adult	♀	—	+	+	+	+	103.6
0519	6/19/18	Adult	—	3	+	+	+	+	Out-patient
4138	6/21/18	24	♀	2	+	+	+	+	100.2
4193	8/27/18	5	♂	3	+	+	+	+	104.0
4213	9/17/18	33	♂	1	+	0	+	0	100.0
4457	12/27/18	25	♂	2	+	+	+	+	103.4
4490[3]	1/11/19	19	♀	2	+	+	0	0	99.2
4514	1/30/19	19	♀	2	0	+	0	+	99.6
4551	2/18/19	21	♀	2	+	0	+	0	100.0
4578	2/28/19	24	♂	1	0	+	0	+	98.8
4583	3/ 4/19	23	♂	2	+	+	+	+	102.2
4598[4]	3/10/19	20	♂	1	+	+	+	+	98.6
4620	3/22/19	19	♂	2	+	0	+	0	100.2
4630	3/27/19	21	♂	2	+	+	+	+	102.4
4634	3/28/19	22	♂	1	+	0	+	0	99.6
4650	4/ 7/19	21	♂	2	+	+	+	+	102.0
4655	4/10/19	21	—	2	+	+	+	+	100.0
4686	4/29/19	22	♂	1	+	+	+	+	99.6
4701	5/ 6/19	19	♂	1	+	+	+	+	99.8
4702[7]	5/ 7/19	26	♀	1	0	+	0	0	102.2
4714[5]	5/15/19	21	♀	2	+	+	+	0	102.0
4730	5/27/19	24	♀	2	0	0	+	+	100.0
4733[8]	5/29/19	23	♀	2	0	0	+	0	99.0
4753	6/15/19	25	♀	2	+	+	+	+	100.0
4800[6]	7/23/19	14	♂	2	0	0	0	0	99.0
5189*	3/29/20	19	♂	9	+	+	+	+	99.0

* Abstracted in this report.

† In this column, ♂ indicates male, and ♀ female.

1. The discoloration or faint redness of the orifice remained after the swelling disappeared.

2. The parotid swellings had disappeared when this patient entered the hospital for right sided orchitis. The left duct was slightly teatulated. While of interest, this case should not be counted. It simply shows that the duct sign may disappear before the complications of the disease are over.

3. Only one observation was made on this patient by a new intern unfamiliar with the sign. This case should not be considered.

4. A limpid mucus discharge was seen to flow from each duct.

5. The left parotid in this case did not become involved. The slight teatulation may have been normal.

6. A case of submaxillary mumps. The parotids never became involved. There was no reddening of the submaxillary ducts.

7. Observation made four hours after the first swelling of the face was noticed. There had been slight soreness the night before.

8. Observation was made two hours after the patient felt swelling or discomfort in the right jaw. There was no swelling of the ducts. This is the earliest primary case we have observed.

swallowing. The duct at this time was not swollen, but signs of beginning inflammation of the duct orifice were seen (redness) later on. No further observations were made on this case. This is the earliest primary involvement we have observed. Case 9 (4702) is the next.

CASE 11 (5189).—March 29, 1920. Male, aged 19. Came to clinic on the ninth day of the disease. There was marked swelling of both parotids. The left was the first involved. Submaxillaries were negative. Steno's ducts are both teatulated and both orifices are very red. The red area measures 2.5 mm. in diameter. The ducts project 2 mm. Around the reddened areas there is a bluish areola. There are no punctate spots in these areas. The openings of the submaxillary glands are negative.

March 31. Ducts the same.

April 1. Parotid swellings have subsided.

April 3. Ducts: Both orifices are still red, 2 mm. in diameter. There are a few bluish spots in these areas. The redness is becoming less marked.

April 4. Ducts: The redness is much paler; only the orifice itself is now red. Teatulation remains about the same as at entrance. All parotid swellings are gone.

April 5. Ducts: Practically all redness has disappeared. Teatulation the same.

April 10. The ducts do not look so prominent; it is almost impossible to distinguish them.

April 12. Ducts and parotids are entirely negative. Teatulation has disappeared. This was a very marked case of mumps; large swellings of the parotid and marked duct signs. The temperature did not go above 98.6 F. the entire time he was in the hospital, but he entered on the ninth day of the disease.

It will be seen that the presence of the duct sign is uninfluenced by the degree of fever. The remarkable involvement of the parotids which may take place in this specific process without an expression in the temperature (Case 11 [5189]) is well known. The same is true of the changes at the periphery of the duct as described above. The sign occurs early in the disease, probably ahead of the parotid swelling in most cases, and persists throughout the course of the disease.

Submaxillary Mumps.—Thus far we have been unable to see any changes in the ducts in submaxillary mumps or parotid mumps in which the submaxillary glands were involved.

Whether the duct sign is pathognomonic of parotid mumps or whether it may occur in any acute inflammatory involvement of the parotid gland, I am unable to say. I have observed a number of face swellings in which the question of mumps arose, two of these acute, in which there was no involvement of the ducts and which later proved not to be mumps.

CONCLUSIONS

1. The duct sign in parotid mumps is described.

2. The duct sign was present in 96 per cent. of the cases recorded and is probably present in all cases of parotid mumps at some time in the course of the disease.

3. Whether the duct sign is pathognomonic of specific parotitis or is present in other acute inflammatory conditions of the parotid gland has not been determined.

4. Because of the occasional occurrence of teatulation of Steno's duct in a certain percentage of apparently normal persons and occasional redness of its orifice, careful differentiation should be made. The duct sign should be regarded simply as corroborative evidence of parotid gland involvement.

DISCUSSION

DR. PISEK: I would like to ask Dr. Cowie how early he has seen this sign, whether he made an examination for it before the parotid swelling appeared in exposed individuals so that we can get some idea how early the duct sign is available.

DR. TALBOT: I have noticed the same sign, but I have sometimes found it very difficult to say whether it was present or not. I wonder at what stage of the disease it comes. I want to emphasize that it is important to have a very good light in order to see it.

DR. HEIMAN: I should like to ask Dr. Cowie if he has looked through the old textbooks. I think this same sign was discussed years ago. Another point in the diagnosis was whether there was more saliva on one side than on the other. Another way to make the diagnosis used to be to have the patient swallow something sour.

DR. SCHLUTZ: Among the negro troops mumps was a very prevalent disorder, and I recall this sign. I demonstrated it before the staff once in a negro, but that particular man did not develop mumps. We did, however, observe it in about 50 per cent. of the cases. Another point noted was that the contagious period of mumps is longer than it is given in the textbooks. It is fully twenty-one days, though it is stated to be shorter than this as a rule.

DR. COWIE: With reference to the question as to the earliness with which the duct sign appears. This point has been considered in the paper. Usually when patients present themselves at the clinic the symptoms of mumps have fully developed. At this time the duct sign is almost invariably present. I have not had an opportunity to watch an incubative case of mumps or one which I could watch before the parotid swelling began. In one case described the sign was present at least before the parotid swelling was easily seen. I have frequently seen the duct sign appear before the parotid swelling was visible in patients who entered the clinic with the involvement of only one side.

Dr. Heiman speaks of an old textbook which describes this sign. I expected to find a description of the duct involvement in the older texts, but was not successful. I should like very much to have the reference.

Dr. Porter speaks of having used this sign in the differentiation of suppurative parotiditis and other inflammatory conditions of the parotid gland. I am very much interested in what he says. I have only had an opportunity of seeing one or two swellings which seemed to involve the parotid gland. In these cases there was no involvement of the ducts. It was not at all certain that the parotid was involved in these cases.

Dr. Schlutz spoke of having seen the duct sign develop ahead of the parotid swelling. As I said before, I have not seen this myself in developing mumps. I believe it will be found that the duct sign, like the enanthem in other contagious diseases, will develop ahead of the parotid swelling.

As to the difficulty of recognizing the sign. As Dr. Talbot says, the spot itself may often be very pale. If the duct is watched from day to day it will be seen to undergo a progressive and retrogressive change. Difficulty arises in those individuals who have under normal conditions a red or pink spot marking the orifice of the duct. It has so happened in all the mumps cases we have watched that the teating and the reddening have undergone changes and the reddening has entirely disappeared before discharge from the hospital.

A CASE OF PRIAPISM RESULTING FROM RAPIDLY SPREADING MYXOSARCOMA WITH GENERALIZED METASTASES*

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REPORT OF CASE

Raymond G. (Case 5140), schoolboy, aged 9 years, entered the pediatric service of the University Hospital March 4, 1920. His chief complaints were lameness and stiffness of the back and neck; stiffness and difficulty in moving the left upper extremity; priapism, which had been persistent for about three weeks; some difficulty in swallowing and in articulating his words because of stiffness of the face muscles and inability to open his mouth freely; disturbed vision; headache situated in the right supraorbital region; difficulty in starting micturition, but no pain.

Family History.—The father, who is a laborer, had an accident six years ago last June: "Some ribs were broken and also his collar bone in two places." December, 1919, he had three marked hemorrhages in twenty-four hours which were thought to have been pulmonary. None since. "He is just as well now as he was before he had the hemorrhages." Mother's father and sister are said to have died of pulmonary tuberculosis. Mother died of what was called typhoid pneumonia. The history seems to show that shortly after Raymond's birth, there was strong suspicion that she was tuberculous. About three months after she was thought to be cured, she developed this fever, "typhoid pneumonia," which continued six weeks, and then she died. Raymond was the first child, born two years after marriage.

Past History.—Patient had measles when 4 or 5 years of age. He had no other infectious diseases. He was a strong baby. As he developed he became "moody," subject to dreamy spells; he would go off by himself and think and seem to be in a dream. He started in school at the age of 6 and advanced to the fourth grade. He always complained a great deal of headaches, cried easily and was hard to cheer up. He began to complain of his neck and back being stiff and aching about a year before entering the hospital. He was better in the warm weather. His "worst time seemed to be between January and May" so that when the present trouble began it was thought to be a recurrence of the same thing. There is a history of frequent earaches.

Injuries: He had been definitely hurt on two occasions, once when he was pushed off the schoolhouse platform, falling three feet, face down; "cried all afternoon saying his back hurt," and once when he had the coasting accident which has been thought to have played a great part in the development of his present illness.

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* From the Department of Pediatrics and Infectious Diseases, University of Michigan.

Present Illness.—About Dec. 28, 1919, while sliding down hill, Raymond had one hand on each runner of the front of his sled, one knee on the back of the sled; with the other foot he was starting the sled down hill when his playmate jumped on his back. He went home screaming with pain in his back and his back was lame for several days. He returned to school. It was thought that after the accident his appetite became poor; that he was easily annoyed; the children playing seemed to bother him; while he played at times, he was not as playful as before. (This detailed account of the accident is given because of its possible connection with the development of the primary growth. Some have taken the view that it would be impossible to hurt the genital organs by such an accident, on the other hand, it is possible that he may have fallen astride the sled and thus injured the scrotum or perineum. There is no history of pain in this region.)

About the middle of January, 1920, he began to complain of pain and aching in his back. He again became stiff and was unable to bend over or to either side or to twist himself. His whole spine was rigid. Severe headaches developed, keeping him awake at night. He also, at this time, complained of dull pain in his knees which has occasioned a limp in his walk, more marked on the right side. About three weeks before entrance to the hospital, priapism developed and has been continuous. There is difficulty in starting urination; this is accomplished twice daily without pain or other abnormality. Soon after the development of priapism he noticed that he was unable to see objects placed on the left of him and that his right eye turned in. The speech and swallowing defect date from the last fall when his jaws began to get stiff. He talks through his teeth without moving his jaw and he swallows with a definite impediment, choosing liquid foods. Difficulty in moving the left upper extremity is of recent occurrence. At times it is almost impossible for him to raise the left arm above the head.

Physical Examination on Entrance.—Slender prominent frame, wasted musculature; practically no panniculus; no edema. There is no play of the facial muscles. The jaw is stiff. The teeth open only 1.5 cm.; if an attempt is made to open the mouth it induces pain. The teeth are carious; *fetor exore.* The patient's body is stiff. The spine cannot be bent and the back muscles are stiff, like a board. He turns his head slightly from side to side, but this is largely accomplished by moving the body with it. He cannot move his head up and down. When he arises to the sitting position the head, neck and body are almost perfectly rigid. If any attempt is made to bend his back in any direction he cries out with pain. He has difficulty in raising the left upper extremity above the head. The other extremities show no limitation of motion. When the thighs are rotated there is pain in the hips. An attempt to rotate the legs causes pain in the knees. Grip in both hands is fair. The patella, ankle and elbow reflexes are not obtained. Babinski is negative; Oppenheim and Brudzinski cannot be obtained. (The knee jerks have been tested on many occasions. At one time they were thought to be present.) Pupils are equal and react promptly to light, slowly in accommodation. There is paralysis of the left external rectus. The patient is unable to rotate the left eye outward. There is no nystagmus. The vision in the right eye is definitely impaired; persons are seen as mere shadows; unable to count fingers or coins. There is definite tenderness on pressure above the right eye. There are no tremors. The other joints are prominent but show no abnormalities. The skin is pale and dry. There is considerable lanugo hair on the face and a slight amount of pubic hair. The glands are practically negative. The inguinal glands are

felt, small. When the patient walks he does so with great care, standing with his body perfectly stiff and favoring the right extremity. When he attempts to pick up an object from the floor he bends at the knees and keeps the back straight.

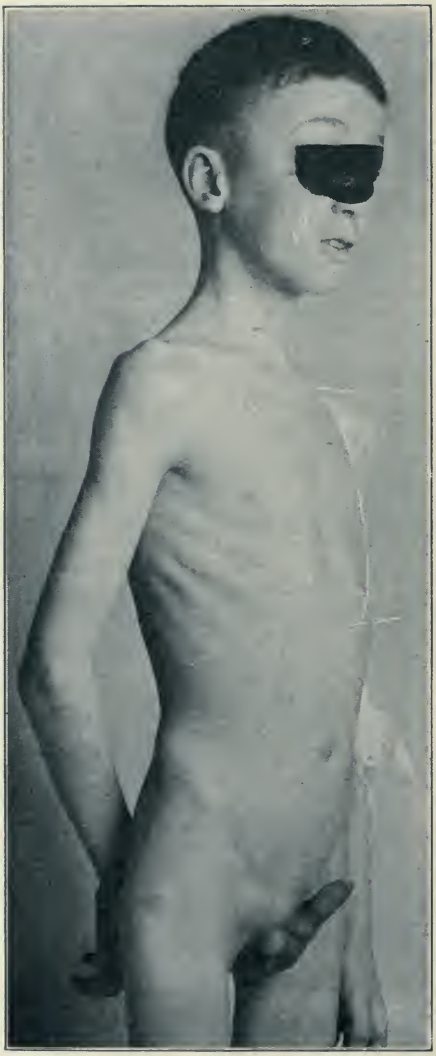

Fig. 1.—Taken soon after the tumor in the scrotum was first visible. The stiffness of back, neck and face muscles is evident; fixation of the jaw and priapism are marked.

The head is symmetrical and presents no abnormal prominences. Aside from the facies it is negative.

Thorax: Juvenile type. Pressure over the ribs at several points shows tenderness, otherwise negative.

Lungs: Percussion negative. Auscultation shows nothing definite. Spinal dullness extends only to the first dorsal. No d'Espine.

Heart: Negative.

Fig. 2.—Showing the marked increase in size of the mass on the left jaw, the frontal nodule, and the nodule to the right of the sternum.

Abdomen: Liver edge at costal margin. Kidneys and spleen not felt. The muscles are held very tense. No hernias.

Genitalia: Priapism is marked, continuous and painful if manipulated (Fig. 1). The prepuce can be retracted. No smegma. Both testicles felt in the scrotum.

Laboratory Findings.—Urine: The urine was examined on many occasions. Aside from high specific gravity it was negative. Urea and other biochemical tests not done.

Blood: March 4, 1920.—Red cells, 5,150,000; white cells, 12,000. Differential count shows polymorphonuclears, 71.2 per cent.; basophils, 4.1 per cent.; large lymphocytes, 17.1 per cent.; small lymphocytes, 7.6 per cent.

March 9, 1920.—Leukocytes, 18,000; hemoglobin, 62 per cent. Arneth count shows slight shifting to the left as follows: Mononuclear, 36 per cent.; binuclear, 35 per cent.; trinuclear, 23 per cent.; quadrinuclear, 5 per cent.; quinquinuclear, 1 per cent.

March 10,—Red cells, 4,400,000; white cells, 20,000.

Spinal Fluid: March 7.—Lumbar puncture in the sitting position; 4 c.c. of clear fluid came away under normal pressure. No more would flow out. Ten cells per field. Definite clouding with carbolic test. Otherwise negative.

March 9.—Lumbar puncture sitting position; 7 c.c. perfectly clear fluid under normal pressure was obtained. Cell count seven per field. Saturated ammonium sulphate negative. Phenol gives a definite cloud, positive. Fehling's test shows a reducing substance present. Collodial gold, 0112210000.

Wassermann: Blood and spinal fluid Wassermann negative.

Tuberculin Test: Repeated von Pirquet tests have been negative with 25 and 50 per cent. solutions.

Reports from Special Clinics.—Otolaryngology: Septic tonsils. Small mass of adenoids. Nasal cavities negative. No evidence of sinus disease. Ears negative.

Opthalmology: Optic neuritis, O. D., paralysis of left external rectus. Pupil, O. S., dilated more under mydriatic than O. D., indicating partial paralysis of the ciliary muscles O. S.

Syphilology: Clinical examination for hereditary syphilis entirely negative.

Roentgenology: Stereoroentgenogram of the head for sinuses shows all sinuses air containing, negative. The sella is normal in every respect. Roentgenogram of jaw is negative. Roentgenogram of spine, shows it to be perfectly normal.

Clinical Notes.—Temperature: Patient had an irregular temperature without any definite type, varying between normal and 101 F. (a few times it reached 102) until March 24, after which it remained practically normal until death, April 8, 1920.

The pulse rate varied between 100 and 140; otherwise nothing remarkable.

March 5.—A roentgen-ray examination suggests some involvement of the left upper chest (there was some suspicion of involvement of this part of the chest on the entrance examination). The spine is entirely negative.

March 8.—Priapism continues. There is a definite small mass in the scrotum posterior to the right testicle. The right testicle is free. The left is felt but is difficult to outline. There is a well circumscribed mass at the angle of the left jaw about the size of a hickory nut. It is fairly firm. The patient is unable to open his mouth more than 1 cm. He has difficulty in pronouncing words. There is nystagmus of the right eye when it is fixed on an object to the left. Knee jerks cannot be obtained.

Provisional Diagnosis.—Malignant tumor in the scrotum with metastasis in bone and cerebrum. The latter probably responsible for the eye signs. The tumor is probably a teratoma.

March 9.—Patient says he has to bear down very hard to start his urine, but there is no pain. The urine is clear.

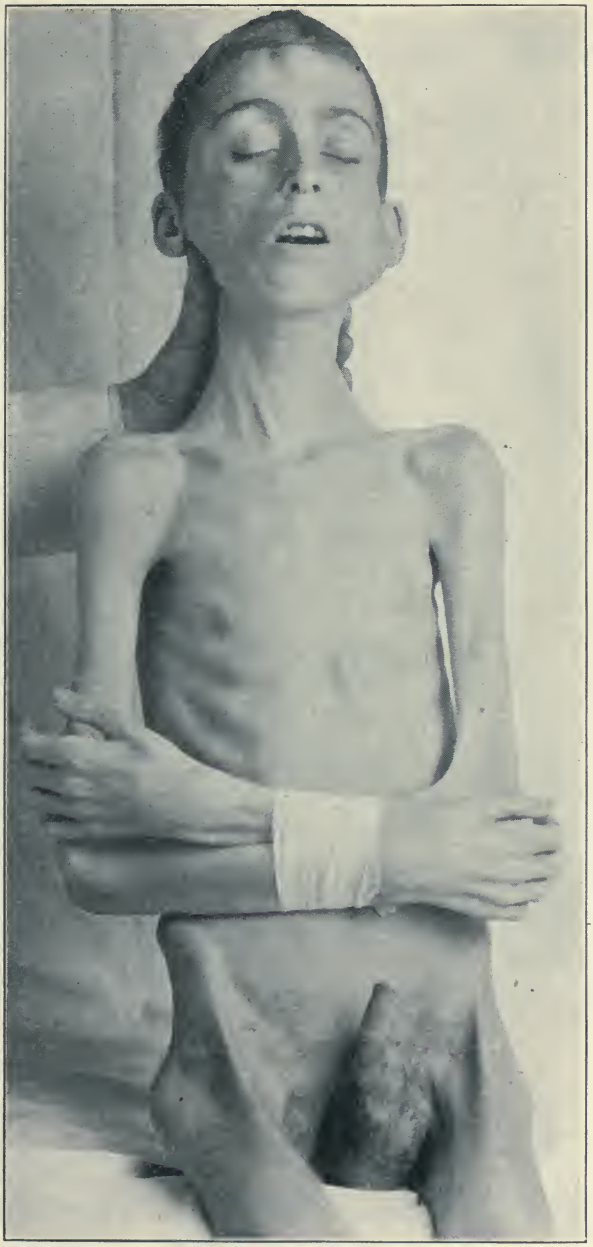

Fig. 3.—Taken soon after death, showing the nodule recently developed on the right jaw and the extent of the scrotal growth.

March 11.—Patient is not as bright as a week ago. Return of his aunt caused no emotional reaction; he made no response to her salutation. He complains of persistent frontal headaches. There is pain on pressure over both supraorbital nerves during the past few days.

Metastases: Swelling half an inch in diameter has developed in the center of the forehead. This is firm and circumscribed. The swelling at the angle of the left jaw (Fig. 2) is increasing and is still firm. There is pain on pressure over the third right costosternal articulation and at the sterno-clavicular joint. Patient complains of his back and calf muscles being sore. He seems to walk a little better.

Fig. 4.—A closer view to show the nodular masses along the penis and prepuce.

March 10.—A large nodule is felt over the left occipital bone 3 cm. in diameter, firm, painful, elevated 0.5 cm. above the skull.

March 18.—The tumor mass in the scrotum is increasing in size. The jaw mass, which receded a bit after the roentgen ray was used, is larger. The teeth cannot be separated as well as before. It is difficult to understand what the patient says.

March 21.—Forehead nodule is 2 cm. in diameter. A smaller nodule has appeared on the top of the head, hard and attached to the bone, slightly tender to pressure. The occipital nodule is larger, very tender. The jaw nodule continues to enlarge; is more irregular. A similar nodule is developing on the

right jaw in the same location. Scrotal mass is larger and is rapidly extending toward the anus. The right inguinal glands are now as large as small almonds. The patient was transferred to surgery service for biopsy.

March 23.—Tumor mass in the scrotum has grown very rapidly and is very hard. Both testes can be felt separate from the mass. A mass in the right inguinal region the size of a hickory nut is now felt (Figs. 3 and 4).

April 1.—A friction rub over the chest on both sides is heard, more noticeable on the right side than on the left. No change in the whispered or spoken voice. There is a small nodule on the third right costal cartilage near the sternum, the size of a large pea. The other nodules are all increasing in size and a new one is developing in the right temporal region which does not seem to be as hard as the others. The tumor mass in the scrotum is extending farther down, and is also beginning to extend up into the body of the penis. Mastication is now almost impossible. Patient is losing weight rapidly. The heart is negative. Patient complains of being short of breath.

Fig. 5.—Skull cap outer surface.

The chest is full of ronchi, particularly on the right side in the axillary region. No definite râles or dulness can be made out. The patient cannot be turned for examination of the back because of great distress. There is still pain on manipulation of the penis and the masses are more marked. Small nodules have developed up to the end of the prepuce.

In general, it may be said that the skull is full of nodules, altogether, large and small, seven are counted. The first one described over the left occipital bone is 4 cm. in diameter; the one over the forehead is 3 cm. in diameter. They project fully 1 cm. above the skull (Figs. 5 and 6).

April 2.—The process can be seen to advance daily. Nodules about the size of peas can be seen to have developed since yesterday. The left testicle seems to be lost in the tumor mass which is very much larger in all directions. Feeding by gavage.

April 7.—There are tubercles all along the penis up to the glans. A nodule has developed on the right superior maxillary, just external to the right orbit.

April 8.—Biopsy Report: Dr. Warthin reports the tissue as an alveolar myxosarcoma, congenital type, probably primary in the bladder.

Fig. 6.—Skull cap inner surface.

The patient is slightly cyanotic this morning. The cyanosis extends down over the shoulders. The heart sounds are masked by the ronchi. The liver and spleen cannot be felt.

The patient died suddenly at noon.

SUMMARY

This is a case of a rapidly developing tumor in the scrotum associated with what I believe to be multiple metastatic growths in the skeletal structures, intracranial changes, indefinite intrathoracic changes particularly on the left side, not involving the heart; with a history of injury which, however, occurred, apparently, after he

first complained of back stiffness, but which may have had an influence in the process. We are thus far unable to determine the cause of the painful rigidity of the back and neck muscles. The patient seemed to be holding himself for fear of being hurt. The boardlike stiffness reminds one of that described by Escherich in his cases of pseudotetanus. This condition, however, is at once ruled out.

Instead of more than one process being at work to induce the different groups of symptoms, I believe the entire process is due to a malignant tumor with bone and visceral metastases. I have seen a number of malignant tumors in children in the clinic. Because of bone metastases we made the tentative diagnosis of malignant teratoma. Dr. Cabot concurred in the idea of malignant tumor and Dr. Warthin, before the child's death, concurred in the probability of its being a teratoma.

NECROPSY PROTOCOL

The following notes are extracted from Dr. A. S. Warthin's necropsy records, made April 8, 1920.

Gross Findings.—There is a great abundance of lanugo hair over the face and upper extremities, nodular masses on the scalp and angles of both jaws, in the center of the forehead, on the costal cartilage at the junction of the third rib. Nodules were also found on the anterior surface of the sacrum. The bodies of the vertebrae were all involved, nodules being found on either side along the entire course of the spine. In the upper thoracic region there was a marked deformity bringing about anterior projection of the bodies of the thoracic vertebrae just behind the esophagus at the suprathoracic straits (this in part accounts for the difficulty in swallowing). The bodies of the vertebrae were infiltrated with the growth, so much so that they could be easily picked to pieces. The masses in the scalp were semi-elastic. The floor of the cranium was also involved in the tumor growth. There was a large soft metastasis involving the roof of the orbit and cavernous sinus on both sides, particularly the right.

Heart: The heart was negative, excepting for pallor of the heart muscles.

Lungs: The left lung was filled with metastases. The right was adherent. Both plueral cavities contained fluid. The fluid was slightly cloudy on the right side. Some of the nodules on the surface of the left lung were from 1.5 to 2 cm. in diameter and elevated 0.5 cm. above the surface; light yellowish in color and resembling a button. One of these was umbilicated. The same buttonlike nodules were found on the upper surface of the diaphragm. The bronchial glands on the left were hyperplastic and edematous. No metastases. On the right they were entirely replaced by metastases the size of hickory nuts. When these were cut through they appeared soft, cheesy and yellow.

Stomach: Negative.

Pancreas: Negative.

Liver: Negative. One area showed a diffuse infiltration.

Spleen: Negative.

Intestines: Negative.

Genitals: The testicles were pushed up into the canal by the scrotal tumor and were not involved in the growth. The bones of the pelvis showed only secondary processes. The bladder showed no growth; the thickening in the wall was all in the subserosa. The primary growth was found in the prostate; the entire gland being replaced by the new growth. The urethra was surrounded by a soft, mushy, purulentlike growth. The penis was almost entirely replaced by the nodular masses varying in size from a buckshot to a pea.

Brain: The central longitudinal sinus contains metastatic nodules in its anterior portion. The circle is negative. The basal meninges are negative. The arachnoid shows irregular thickening between the convolutions. The meninges strip with difficulty, markedly edematous. There are adhesions between the arachnoid and the cortex. The ventricles are negative. The brain substance shows anemia but no metastases. The cerebellum, medulla and cerebral cord were edematous. The hypophysis was atrophic. The sella was nearly filled with neoplasm. The brain weighed 1,330 gm.

Microscopic Findings.—Brain: Congestion and edema. No metastases in brain substance.

Cranium: Metastases in scalp, cranium and floor of skull. Show a picture of round cell alveolar sarcoma.

Vertebrae: All metastases show the picture of an alveolar round cell sarcoma.

Heart: Simple atrophy. Fibroid atrophy. No neoplasm.

Clot from Heart: A laminated mixed clot containing nests of tumor cells.

Aorta: Slight fatty degeneration of the intima.

Lungs: Purulent bronchopneumonia with numerous streptococci colonies. Numerous metastases, some of round cell and others of an oat-seed spindle cell histoid sarcoma. The centers of the metastatic growths show marked tendency to caseous necrosis.

Bronchial Lymph Glands: Show metastases. Calcareous healed tubercle.

Prevertebral and Mesenteric Nodes: All filled with metastases. Some of the large mesenteric vessels contain masses of tumor cells. The prevertebral ganglia and the roots of the spinal nerves are surrounded by masses of tumor cells.

Thymus: Many large corpuscles of Hassal.

Thyroid: Abundant colloid. No metastases found.

Tonsil: Moderate hyperplastic tonsillitis.

Spleen: Simple atrophy. Congestion. Thrombosis of splenic vessels. Small metastases in some of the splenic follicles.

Suprarenals: Atrophy. Slight lipoidosis.

Kidneys: Slight cloudy swelling. Congestion.

Pancreas: No metastases.

Liver: Slight atrophy. Cellular infiltration of some of the periportal islands.

Stomach: Simple atrophic catarrh.

Colon: Slight mucous colitis.

Appendix: Negative.

Small Intestine: Slight catarrhal enteritis.

Urinary Bladder: Slight chronic cystitis. Diffuse infiltration of the wall with neoplasm.

Prostate: No prostatic tissue can be recognized. Completely replaced by alveolar round cell sarcoma.

Penis: Corpora cavernosa and corpus spongiosum infiltrated with round

cell alveolar sarcoma; in many places by cells of an oval or oat-seed shape. Numerous areas of simple caseous necrosis.

Hemolymph Nodes: Numerous phagocytes containing hemosiderin in sinuses.

Final Pathological Diagnosis.—Alveolar oat-seed sarcoma, primarily a myxosarcoma, arising in region of prostate. Infiltration of cavernous spaces of penis with chronic priapism; erosion of pubic bone; infiltration of bladder wall; multiple metastases in skull, vertebrae, ribs, sternum, lungs, pleura, diaphragm, spleen and lymph nodes; infiltration of cranial and spinal nerves and sympathetic ganglia; free ball thrombi containing neoplasm cells in right heart; thrombosis of retroperitoneal and splenic vessels with tumor cell embolism; terminal acute bronchopneumonia; general marasmus; fibroid atrophy of thymus; hemosiderosis of lymph nodes; postmortem pseudomelanosis.

The stiffness and sensitiveness of the back are now explained by the necropsy findings along the course of the spinal column.

REPORT OF A CASE OF ANAPHYLAXIS FOLLOWING AN INTRADERMAL PROTEIN SENSITIZATION TEST*

H. J. GERSTENBERGER

CLEVELAND

During July, 1919, I was called in the absence of the family physician to see, in the words of the mother, "whether I could not change something in the diet or care of her child that would remedy or lessen the irritated condition of the skin and the wheezing heard during breathing."

I found a quite well developed and well nourished boy, aged 12 months, with signs of a mild rickets, prominent forehead, slight beading of the wrists, with a distinct but mild dry eczema of the face, chest and arms, causing, as one could see from the many scratch marks, a great deal of itching and with a decided emphysema accompanied by wheezing and a somewhat labored expiration. The spleen was not palpable and the posterior cervical lymph nodes were somewhat increased in size and number, as is usually the case in exudative children. The skin symptoms were first noted by the mother at about the age of 7 months, while the respiratory difficulty never, until recently, made the impression on her of a decided abnormality, although she recalls now that since the boy was about 2 months old she noticed that there was something about his breathing that was not just right.

The boy was breast fed until about three weeks of age. Then he was fed a Walker-Gordon mixture by the family physician, and at the age of 9 or 10 months he was given straight milk with vegetables. He received orange juice early, but was given neither eggs nor potatoes. When the eczema developed the diet was changed in various ways without definite results and so the family physician consulted a dermatologist.

The skin at that time is reported to have evidenced a marked moist eczema, which improved but was replaced by a dry, scaly, itchy skin which remained uninfluenced by further treatment until June, 1919, when it improved without any special change in the diet or treatment.

When I saw him one month later at the age of 12 months I ordered less food, skimmed milk as the basis of the diet, atropin sulphate, in 1 : 1000 solution, gradually increasing the drop doses to the point of physiologic reaction, and a 10 per cent. tricalcium phosphate mixture in cod liver oil. A cutaneous protein sensitization test was suggested at this time in case the therapeutic measures instituted should be of no avail.

However, a decided improvement in the skin and chest symptoms was soon noticed by the mother and nursery maid. The diet was kept the same in quality, but increased in quantity to meet the appetite of the child without causing an increase in the symptoms. The latter, on the contrary, continued to grow less and less and at times seemed, at least to the mother and nursery maid, to be entirely absent.

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The nursery maid who had constant care of the child was convinced in her own mind that the atropin was responsible for the improvement, for not only had she noticed that the child began to improve after the atropin had been started, but she also felt that a return of the symptoms occurred when the atropin was reduced or stopped, as occasionally happened.

The family physician returned in August, 1919, found an increased thymic dullness and requested a roentgen-ray examination of the chest. A wide shadow was found in the thymic area which the roentgenologist pronounced an enlarged thymus. Consequently, the family physician stopped the atropin and had the thymus roentgenized once every three to four weeks for five times. The condition of the child got worse instead of better and the thymic shadow remained the same, so that the roentgenologist advised against further exposure. The family physician then reordered the atropin in the form of belladonna in small doses. The child improved once more and gradually during the latter half of November breathed, according to the family, in an almost normal manner.

During the first days of December he developed a severe cold and as a result had a severe asthmatic attack during the night of December 3. On the following morning I saw him with the family physician, and then he was admitted to the pediatric service of Lakeside Hospital for diagnosis and treatment.

His condition seemed worse then than at any previous time, especially was the cyanosis decided on slight exertion and this was accompanied by an increase in the shortness of breath. At the hospital his diet was again built around skimmed milk, the atropin was reordered in large doses and the cod liver oil continued. In forty-eight hours there was a distinct improvement in the shortness of breath and the degree of cyanosis, although increased activity was still able to increase both symptoms.

The tuberculin and Wassermann tests were negative, although the former showed a slight swelling which, however, was so uncharacteristic of the regular positive intracutaneous tuberculin test that it was considered to be due to the local trauma. The blood count was 4,960,000 red cells, 15,000 leukocytes, hemoglobin, 90 per cent. The differential count gave 35 per cent. polymorphonuclear neutrophils, 51 per cent. small lymphocytes, 7 per cent. large lymphocytes, 6 per cent. transitional cells, and 1 per cent. eosinophils.

The boy's brother had been exposed to whooping cough and the patient had therefore received from the family physician two injections of Pertussis vaccine. A third one was given him on the second day during his stay at the hospital.

December 5 the roentgenogram showed a decidedly smaller shadow than the last one taken during October. In fact, the shadow was quite like that of a normal child. In consequence, the family physician was convinced that the recent improvement noticed during November was really due to the reduction in size of the thymus and not to the influence of the atropin. He was especially convinced of this because Nov. 10, 1919, he had his assistant perform cutaneous scratch tests with different proteins in simple saline solution, which all proved to be negative. No potassium hydrate was used.

The proteins used were: wheat, cow's milk, rice, potatoes, egg white, beef, oats, tomato, horse hair, pneumococci, staphylococci and rag weed. However, as I recently had had the same negative experience with the scratch method in the case of another asthmatic child, and a positive result with the intracutaneous method, it was decided to apply the latter method in this child also, before concluding that the entire clinical picture in this case was due to an enlarged thymus and not to a state of sensitiveness to proteins or to an exudative diatheses, vagotonia or status lymphaticus.

December 8 intracutaneous protein sensitization tests were made with oat protein, cow's milk casein, egg yolk allergen and egg albumin, preceded by a control with physiologic sodium chlorid solution. The solutions used at the first as well as at the later tests were all made in the same approximate manner so that they were probably about the same strength. Later on a scientifically accurate determination was made of the protein contents of a solution made up as closely like the original solution as it was possible to do, with the result of a finding of 1.2 per cent., so that a variation of from 1 to 1.5 per cent. might be probable. From 0.1 to 0.2 c.c. were injected, enough to make a wheal varying in size from a lentil to a match head. The child cried from the beginning of the injections, which consumed more time than was really necessary owing to the fact that the solutions were prepared between the individual injections.

It was noticed as the injections went on that the cyanosis was distinctly increased, but no alarm was felt as it was customary for the patient to become mildly cyanosed on slight exertion, and this experience was considered to be more than "slight exertion," and therefore caused no astonishment in the production of a more marked cyanosis.

The first injection was the control with physiologic sodium chlorid, then followed in order, oat protein, cow's milk casein, egg yolk allergen, and egg albumin. After the egg yolk allergen had been injected and while the egg albumin was being administered the cyanosis and dyspnea suddenly became severe and extreme. Epinephrin was immediately administered subcutaneously in repeated doses, totaling about 1 c.c. While the respiratory difficulty was at its worst, a pale swelling about the size of a quarter of a dollar was seen at the seat of the egg yolk allergen and egg albumin injections.

The areas of administration of the oat protein and cow's milk casein were absolutely negative. Inasmuch as the cyanosis and dyspnea, except for the final extreme severe period, developed slowly and gradually during the periods of injection, it was our impression that the aggravated condition of the child was not due to a condition of anaphylaxis, but rather was the result of the increased physical effort in struggling.

We imagined that we had produced a severe and acute mechanical emphysema by forcibly pumping the child's lungs full of air beyond the relative constriction of the bronchioles, which, of course, was known to have existed from the beneficial effects that atropin had had on the child's condition before the injections had been made.

The powers of the factors of expiration being smaller than those of inspiration, one could understand how gradually with each inspiration more air could have been forced into the lungs than was let out during expiration, resulting finally in the fixation of the chest in the inspiratory phase. On the following day, however, the child developed a very marked and general urticaria, which required for its improvement hypodermic administration of epinephrin. The appearance of this symptom made the diagnosis of anaphylactic shock more probable as the cause of the acute difficulty of the day before.

Nevertheless, it was decided after a few days of rest to repeat the test, but modify the procedure by having the syringes ready and loaded with the proper solutions in order to use as little time as possible and avoid undue exertion on the part of the child. This idea was carried out further by reducing the number of proteins to be tested to three.

December 11 cow's milk allergen, cow's milk casein and cow's milk albumin were injected in the same solutions as were used in the first observation. One of the lesions showed a pale swelling, but on the following day a raised red indurated area, about the size of a bean, was seen at the seat of the cow's milk allergen injection, while the cow's milk casein and cow's milk albumin showed but a very faint and slight induration which was considered absolutely negative.

The test was performed in a very short period of time and caused the child only slight difficulty and annoyance.

On the following day, December 12, the proteins of orange, tomato and strawberry were injected in the same manner and with the same rapidity as on the previous day. No urticarial wheals were seen and only a slight induration such as was noticed at the seat of the cow's milk casein and cow's milk albumin injections of the day before was observed at the point of administration of the tomato. No reaction at all was found where the strawberry and orange proteins had been applied. The technic again worked perfectly and the child went through the tests with only slight difficulty.

As a result of the good experiences of the last few days, it seemed as if possibly after all the mechanical factor of an acute emphysema produced as the result of the prolonged exertion and crying of the child had been mainly responsible for the extreme condition of the first day. Of course, the factor of anaphylaxis could not be excluded and so it was decided to inject only one of the two proteins which produced urticarial wheals on the first day, namely, egg yolk allergen and egg albumin. The former was chosen and was injected the following day, December 13, quickly and carefully without any difficulty or inconvenience to the child.

The resident physician who had performed the injection remained for a few minutes and then left. The nurse had placed the child in bed and after about five minutes went out of the room for some water. She returned immediately and discovered the child breathing with the greatest difficulty and extremely cyanotic. The resident physician was called and found the child in a state of apnea and marked cyanosis. He administered epinephrin and started artificial respiration. A total of 2 c.c. of epinephrin was injected subcutaneously. The child recovered. A large urticarial wheal was seen at the point of the egg yolk allergen administration and likewise at the areas which on the first day, December 8, had shown urticarial wheals, namely, the point of injection with egg yolk allergen and egg albumin.

This experience settled beyond question that the extreme condition of the child December 8 was due to anaphylaxis and that the mechanical emphysema, which from the clinical picture did exist to a medium degree before the administration of the egg proteins, was at most a minor factor. The child had never received egg in any form, so we are justified in assuming that this hypersensitiveness was congenital.

The family history regarding the older brother, the parents and the grandparents is negative to asthma, eczema and hay-fever.

Although the amount of protein administered at the individual injections was small, it nevertheless must be admitted that the dosage was probably somewhat above the upper limit of safety for a child of this type. However, I

believe that had we injected one-tenth or one-twentieth of the amount used, which would have been beyond all criticism, we still would have witnessed the development of a severe and serious anaphylactic shock.

We appreciate now more than ever the value of epinephrin, not far away but close at hand. Had these tests been done at home and in the absence of epinephrin, we should have reported today a fatality instead of a recovery.

December 16 another roentgenogram of the thymic region was made and it showed an abnormally wide shadow. The technic employed as to the position of the child and the condition of the tube was proper and the same as used in previous exposures.

A fluoroscopic examination demonstrated that this seeming contradiction in the roentgenogram depended on the phase of respiration in which the picture was taken, a picture made during extreme inspiration giving a practically normal shadow and one taken at extreme expiration a markedly abnormal one, as large, if not larger, than that recorded in the plates of Aug. 5, 1919.

COMMENT

The following points in this case seem to be of interest:

1. A boy, 17 months old, who had never received egg in any form developed an extreme anaphylactic shock after an intracutaneous administration of egg yolk allergen and egg albumin in doses of from 1 to 2 mg.

2. That a seventeen months old boy who had received cow's milk since his third week of life and who had suffered from eczema and asthma showed a negative intracutaneous test to cow's milk casein and cow's milk albumin, the former having been injected twice within four days. The intracutaneous injection of cow's milk allergen responded in twenty-four hours with an indurated and red area of infiltration that was not unlike that of an ordinary positive von Pirquet test, but entirely different from an urticarial wheal.

3. That this same boy also was not sensitive to other proteins such as oats, strawberries, orange and tomato.

4. That the first severe anaphylactic shock of December 8 did not prevent the production on December 13 of a second following the administration of egg yolk allergen five days later. In other words, this boy did not develop a state of anti-anaphylaxis as a result of his anaphylactic shock. In this connection it is suggested that at no time should sensitization tests, according to the intracutaneous method, nor injections of serums subcutaneously, be made without having adrenalin close at hand. Such a precaution might have saved some of the fatal cases reported.

5. That the roentgenograms of the boy made at different intervals on the same day show a definite, wide, abnormal thymic shadow and again a perfectly normal picture. The former as found by fluoroscopic examination occurring during extreme expiration, the latter during extreme inspiration.

6. That the enlarged thymus, if it really be large in an abnormal sense, did not produce the respiratory difficulty in a mechanical way.

7. That this patient may be a case of status lymphaticus and this condition may be responsible in him for his congenital pathological sensitiveness to egg proteins and for his anaphylactic reaction. If, however, he should be found not to be sensitive to other proteins, especially to horse serum and horse hair protein, the status lymphaticus could hardly be accepted as a causative factor in his condition, for it would be difficult to imagine how a status lymphaticus could make a child sensitive solely to egg protein and not to some other proteins, as milk, strawberry, oats, and especially horse serum or horse hair proteins.

DISCUSSION

DR. TALBOT: Of course, it has been known that children with eczema are peculiarly prone to sudden death, and children with eczema are prone to have large thymus.

When one looks at the roentgenogram of the thymus he is looking through the shadow and it does not tell him how deep the shadow is, so that one cannot say that he has not a pathologic thymus because the roentgenogram does not show it to be enlarged.

DR. DEBUYS: How and how much epinephrin may be administered?

DR. TAYLOR: Did you give the protein tests cutaneously or intradermally?

DR. GERSTENBERGER: I appreciate that an increased anteroposterior diameter theoretically may be a factor in causing respiratory difficulty. I am likewise aware that the literature contains this idea, namely that an increase in the anteroposterior diameter of the thymus may be the cause of the respiratory difficulty and may be present without an increase in the lateral dimensions. However, unless such cases are given the opportunity to show under the fluoroscope whether or not they can develop a wide shadow, one cannot conclude that the respiratory difficulty was due to an enlarged anteroposterior diameter, and as is pointed out in the paper itself it is a question whether the presence of an enlarged diameter of thymus is after all the cause of the respiratory difficulty.

So far as this specific case is concerned this question need not arise for we have seen that it is possible to produce in this child at will a very wide and seemingly abnormal shadow by causing him to go into forced expiration.

Again, on the other hand, I wonder whether some cases that have been diagnosed as enlarged thymus are not normal cases which show a somewhat wider shadow than normal in the thymic region possibly because the photograph was taken just at the end of a prolonged forced expiration.

As to the epinephrin, we gave, in divided doses of from 0.2 to 0.3 gm. a total of 1 c.c. the first time, and then a total dose of 2 c.c. at the second attack.

We used the intradermal method because the cutaneous scratch method did not give results. We did not, however, use potassium hydroxid in performing the latter test.

I want to emphasize the great advisability of having epinephrin at hand whenever you perform intracutaneous protein tests or following the injection of horse serum for I am convinced that certain cases of death following the injection of horse serum could have been prevented by the use of adrenalin at the time when severe anaphylactic reactions have occurred.

FURTHER DEVELOPMENT OF INFANTS' HOSPITALS

'ON SHORE' DEPARTMENT OF THE BOSTON FLOATING HOSPITAL

HENRY I. BOWDITCH, M.D.

BOSTON

The present day tendency among hospitals is to develop the scientific side and its laboratories so as to bring them closer to the clinic. This valuable information must be weighed properly to be of true service, for we are dealing with the delicate human body and mind, not test tubes, and common sense and experience play an important rôle.

Social service, with its home and family findings, necessarily modifies our treatment, and in our prognosis and subsequent handling it must always be remembered that we are dealing in pediatrics with the human family, and that our treatment in a big way has to do with the family mentally as well as our little patient physically. Therefore, why should we spend so much energy in trying to make the child grow and develop normally, considering the first half, while we neglect to see that our efforts are realized and make sure of the proper after care.

The beginning of this new development, made possible through the generosity of a few friends, is being exemplified in the new home of the "On Shore" Department of the Boston Floating Hospital.

SIZE

The plan was worked out on a basis of a ten bed clinic. Ten patients, we felt, were the best number, being more readily possible to follow closely clinically, scientifically and socially. We could get in better personal touch with the parents, and not forgetting the patients, get them discharged the quicker, following them up by our "family control."

This clinic was held in two wards and the necessary isolation room, under the expert care of three nurses.

It is to be noted that as it worked out the children, so divided, got perfect naps morning and afternoon; in dividing the wards there was less noise; and symptoms dependent on restlessness, vomiting, etc., seemed to be markedly diminished.

This clinic was manipulated so as to give us approximately five new patients monthly. We thus had about one week to decide probable cause of the trouble, and then within two or three weeks could prove our point and get a gain in weight before child was discharged.

The scientific laboratories, chemical and bacteriological, were brought into close proximity, making consultation easy; but carefully separated so that natural odors, noises, etc., did not penetrate. Collection of excreta and metabolistic tests were carried on with little difficulty and no mistakes.

EQUIPMENT

Our equipment is composed of three small buildings, each comprising three apartments. These buildings communicate on the first and second floors, protected by fire partitions, and on the top floors.

"The Clinic" (middle building).—This is the main entrance. The first floor is made up of a waiting room, with information desk, lecture room, and educational library; an admitting room, where weighing, measuring and examinations are made; a physician's office for outpatient work; together with a demonstration room and kitchen for instruction of the mothers, etc.

Patients are admitted at all times.

On Tuesday afternoon of each week a health clinic, composed of 150 families, is held under the guidance of an assistant visiting physician; on Wednesday afternoon the return "family control" clinic is held, in charge of the visiting physician.

These two clinics comprise weighing the children, getting clinical history, and giving treatment. The demonstration room and kitchen is used, when necessary, for perfecting the home care.

On the second floor are two wards and one isolation room, seven and three beds, respectively. Here is also a small bath and treatment room for examination of house patients. Out-of-door air treatment is possible on well constructed fire escapes and the roof. The nurses' control desk, chart space, medical and linen closets, lie between the two wards.

On the third floor are adequate, simple sleeping rooms for servants.

Offices and Scientific Laboratories Department (right hand building).—On the ground floor are offices, including secretary's room, resident physician's room, a record room and library, and clinical laboratory.

On the second floor, well equipped chemical laboratories and a small diet room for the house patients.

On the third floor is the office of the research director, bacteriological laboratory and reconstructed milk laboratory. The research laboratories are under the guidance of the director, who controls the research department and carries on the scientific side of the clinic in cooperation with the visiting physician.

"Nurses' Home" (left hand building).—This building is made up, on the first floor, of sitting room for the nurses, also dining room and kitchen.

On the second and third floors are adequate rooms for nurses, and an extra ward.

RESULTS

Since the opening, Dec. 15, 1919, we have received thirty patients, comprising one case of bronchopneumonia, one premature birth, one case each of pyloric stenosis, scurvy, acute rickets, dysentery and eczema. The remaining twenty-three were diagnosed as malnutrition in different degrees, requiring regulation of feeding.

It was our plan to admit only nutrition cases, infection being carefully guarded against. The nutrition cases received included disturbances of the first and second years of life, scurvy, rickets, spasmophilia, digestive disturbances including malnutrition without underlying disease.

Our study so far has been to organize methods of attacking the question of the different food elements in growth or lack of growth. Each case was to be completely examined clinically, chemically and bacteriologically. The incidence of intestinal flora has been watched in the past two or three months with interesting results.

Our plan is to have our patients return, at definite periods, for chemical and bacteriological tests, physical and mental examination, for ten years. In this way we follow the development of the body and mind.

A weekly clinic to meet the parents has proved satisfactory in this small clinic, allowing the personal touch to impress parents with the importance of physical care, proper dietetics, and discipline. In time groups of parents, developing along national lines, will be formed. In this way we hope to understand the mental capacity of the parental group and adapt our ideas to their particular peculiarities; thus com-

prehending the good points of the diet, life, etc., of the different races; and hope to lead them into a better understanding of child life.

This completes the report of the work so far undertaken and we hope that this beginning may lead others to establish similar "small enough" institutions for the same study, for the protection of our medical work.

DISCUSSION

DR. GERSTENBERGER: Dr. Bowditch is to be congratulated on the way in which he has worked out the space at his disposal. It is sometimes just as much fun to do this in an old building as it is to build a new hospital. I think the great satisfaction has come not so much because the place is small as because it was of a size that one man could care for well.

DR. BLACKADER: What does it cost per capita, or what are the expenses of maintenance per month of a small hospital like the one described? I am interested in knowing, for we may in Montreal make a similar venture.

DR. DEBUYS: Dr. Bowditch said something about the cost being $45,000. Was that equipment only or did that include the building? What does it cost per year to maintain the institution?

DR. EATON: In what part of Boston is this hospital located? What about the budget?

DR. ADAMS: I am one of a committee which is spending about $75,000 in remodeling and cleaning up a hospital that has been standing since 1878, and has had very little done to it. Our report as to what this remodeling is going to cost is very discouraging and we have planned for only what is absolutely necessary. The Children's Hospital costs us $1.60 per day; from the city we get $1 and we have to raise the rest by voluntary contribution. The proposition has been made to tear down the hospital and build a new one, but we have built two wings in the last six or eight years and are now getting money for an observation ward because we have had to close the hospital three times for six or eight weeks because of an epidemic. When this proposition to build a new hospital was submitted, it was suggested that the way to raise money was to sell out the whole plant, and get out and buy ground and build a modern hospital. It was found that the ground would net us $125,000 and on further investigation we found that the present hospital was worth $550,000. The committee decided that this was impracticable.

It would be interesting to know what it costs to build and run a small hospital like the one Dr. Bowditch describes. Of course, where you have eighty or one hundred patients in the hospital you cannot make an estimate as to the cost of maintenance on the same bases as where you have only a small number of patients. I would like to know how much capital you have to have. It is not always easy to get the money; we are not all good at raising money. Dr. Chapin knows how to get it out of people. He is always able to get all the money he wants for the Postgraduate Hospital.

DR. BOWDITCH: I can say at the present time that during six months it has practically cost us $12,000 to care for and treat thirty patients, this includes four nurses, one superintendent, two servants, three chemists, one bacteriologist and one clinical physician. The staff is composed of a visit-

ing physician, an assistant visiting physician, a director of laboratories, two assistant chemists, an assistant bacteriologist, an orthopedist and a dentist, for preventive orthopedics and dentistry. We are trying to follow along the question of dental caries, etc., among our problems, and to keep these children under observation for ten years. Of course, the success of the experiment will depend on whether the children will come back and what porportion of them can be held for these ten years. That depends greatly on the personal touch of the physician.

We should get perhaps sixty cases a year which in ten years will come up to 600, so that at the end of ten years we can really begin to talk.

THE EFFORT SYNDROME IN CHILDREN

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It has long been my observation, that children divide themselves into groups as relates to their individual characteristics. This tendency to grouping is not discernible to any extent among infants. After the second year, individual traits, and a distinct personality, manifest themselves. At about this period the child begins to individuate.

During the late war, English army surgeons learned that, when certain recruits were put to prolonged hard work, at drill, hikes and other exertion, they failed to measure up to the endurance standard required of a soldier in the field. These recruits had passed the various physical tests, and had been put to training. After a time it was found necessary to disqualify the men, because of inability to perform the duties and bear the hardships demanded, which others were able to meet. To this condition, Dr. Thomas Lewis applied the term "effort syndrome."

As the most prominent symptoms involve the circulatory and nervous system, later writers have used the term "neurocirculatory asthenia or neurocirculatory myasthenia" (MacFarlane). It was found that in some individuals, the disability was due to infection from the tonsils, teeth or other foci. Other cases apparently were of endocrine origin. To describe the condition, as it occurred, in a great majority of soldiers, Lewis applied the term "constitutional."

Friedlander and Freyhof [1] reported on fifty cases of so-called "constitutional neurocirculatory asthenia."

Robey and Boas, after an intensive study of a large number of soldiers suffering from neurocirculatory disorders, were obliged to recommend for permanent discharge 87 per cent. These cases all belonged to the so-called "constitutional" class.

The boy or girl, who may qualify for the "effort syndrome" class, comes with a typical story, which, condensed, means that there is an absence of capacity for sustained effort, both mental and physical. It is

1. Arch. Int. Med. **20**:648 (December) 1918.

stated that the child is backward in school, behind in his classes. He is intelligent but cannot apply himself sufficiently to become an average student. In like manner he is physically unfit for the usual activities of boyhood. He tires readily and prefers to be a spectator rather than an active participant in games and other amusements. Wherever endurance is required, he fails. If he attempts in later life to make the football or baseball team, he is turned down by the coach or trainer. Nevertheless, he is not ill, and even on a very thorough physical examination will fail to show disease.

The weight and height apparently have little to do with the condition. In my case records this type of child has been heretofore classified as a "poor individual." One of the distinguishing characteristics is a lack of nervous control. The individual boys and girls of this type are subjected to a good deal of unjust criticism. They are accused of being lazy, indifferent, careless and dull. The fact is they are poor types of humans, of from 50 to 75 per cent. capacity.

It is important not to confuse these young people with those who suffer from bad habits, as regards their sleep, rest and general hygiene, or with those who are bodily ill, or with those, who, because of rapid growth and arduous duties are temporarily but not permanently below normal. With suitable management in such cases there will always be a sustained response.

It can be readily understood that in girls the above mentioned constitutional peculiarities may attract less attention and be more readily excused when present.

REPORT OF CASES

CASE 1.—A young man, now 23 years of age, came under my care at the age of 6 months. He was the oldest of three children and the only boy. The father was in fair physical condition, the mother was delicate in the sense that she had very little resistance or stamina. Frequent rest cures were necessary. She had backaches and headaches habitually, was nervous, thin and pale, and always had been a care to her parents.

The boy had the usual illnesses of childhood. He suffered considerably from digestive disturbances in the early years. He was irritable at home and rather unhappy in school. His school life proved very strenuous and was interspersed with frequent intermissions for one cause or another. Mental control was defective. Tantrums were not unusual. As he grew to older boyhood, various boarding schools were attempted, but he never remained longer than the Christmas vacation. It was uniformly found by the head master that the school was not suited to the boy.

When the United States entered the war, he volunteered in a certain department and was accepted, passed the physical examination, and remained a few weeks. He was then advised by the commanding officer that he would do better

work in another division of the service. Thither he went, and was examined and again accepted, but in a short time was advised to apply to another department. Again he was accepted and again he failed. The boy was anxious to enter the service, as all his friends had volunteered and two younger sisters made his life miserable by their anxiety to have a big brother hero.

It was absolutely impossible for this boy to do the work required of him in any of the positions he attempted, although he was most anxious to serve.

These individuals finally drift into the right occupational sphere, one that requires very little expenditure of effort.

CASE 2.—A boy who was a fine physical specimen was frequently ill in early boyhood, but never seriously ill. He had a tendency to be introspective and moody. He did not like school and could not get along very well with other boys. His school attendance was interrupted by headaches, attacks of indigestion and various nervous disorders, he was inclined to hysteria and brain storms. When he was 12 years of age he was ashamed to go to school, because he was so far behind others of his age. With private tutoring he was able to enter the primary department of a large boys' school, at the beginning of the autumn term. Just before the Christmas holiday the mother had a letter from the head master, telling her that in his opinion their particular school was not suited to the requirements of her son. Study made his head ache. Work in the garden produced dizziness. As a young lad he would ride his bicycle down hill two miles to the village, and pay some public conveyance to take him and the bicycle home. He suffered from palpitation if he rode up hill on his bicycle.

He is a well meaning, well spoken, kindly disposed young man, without a trace of initiative. He has tried very hard to be a real boy, but he tells me he cannot, and it has caused him a great deal of worry. Thousands of dollars have been wasted on him up to date. The mother was 46 years old when the boy was born and the father 50.

CASE 3.—A young man, 20 years of age, is still in the preparatory school, preparing for college. I have known this boy since he was an infant, and I have exerted all the influence I possess to have him give up the college idea and go into business. His friends are all in college and there only will he be happy. He enjoys fairly good health, but has never been known to take part in any sport. He prefers to be a spectator. Exertion makes him nervous and any unusual event causes him to remain in bed the next day. He is totally devoid of initiative. The mother of the boy is an habitual invalid, but is never very ill. The father is an unusually able business man.

CASE 4.—A girl, 18 years of age, large, well formed, mentally alert, is in school about half the time. She has frequent headaches and backaches and tires easily. Other girls make her nervous. Parties tire her. An evening of dancing could never be considered. The girl is normal physically and has been examined and treated by a goodly number of physicians. I have known her since she was 2 years old. She always has been and always will be just useless.

These few cases are given simply as illustrative of the type. Similar cases and others less pronounced exist in all communities, and all have one feature in common, a lessened capacity for sustained effort. From the standpoint of treatment they constitute a most discouraging group.

Rest cures, change of climate and various supporting measures are of little avail. As these individuals are fashioned, so they remain.

The poor individual exists throughout the entire animal world. Among the lower animals those of defective capacity, for economic reasons, usually have a short career.

The defective functionating human, if well born, is urged and forced and stimulated to accomplish that which is not in him. *It is impossible to get out of any piece of machinery work which the machine was not intended to accomplish.*

Millions of dollars are wasted on youths who are physically and mentally unable to meet the standards set up by ambitious parents and friends in an effort toward their so-called higher education. The highly trained teaching talent of our preparatory schools and universities is wasted in part on poor student material, from 25 to 50 per cent. of which should be scrapped and put to productive occupation.

Before a boy is permitted to avail himself of unusual educational advantages it should be determined that he is worth it. The high school and the preparatory school should serve as a clearing house. In addition to the mental attainments required for a college entrance, it should be required that a candidate submit testimonials as to physical fitness and mental capabilities from the head master or high school principal. What is needed for economic reasons is expert occupational diagnosticians, who will aid in placing the boys at work to which they are fitted.

I have had the opportunity to keep in touch with a great many boy patients, through manifesting an interest in them, and have been able to advise and assist them along occupational lines. A boy who belongs in the class under discussion should discontinue school in the fifteenth or sixteenth year and take up business. In order to make a reasonable success the occupation must be one that is not strenuous. Such boys often make fairly good salesmen, clerks and bookkeepers. They never get very far, however, as they belong to that considerable class who watch the clock. Advancement in salary, partnership, etc., go elsewhere.

It is exceptional to find children of this type the offspring of strong vigorous young persons. In a great majority of the cases they are the offspring of a weakly mother, the woman of little resistance, of lessened endurance capacity. A strong vigorous mother will do much to

offset the unfavorable influence on the progeny of a weakly male. The progeny of vigorous males is greatly handicapped by inferior mothers. All of which applies to the lower animals as well as the human.

Frequent child bearing has apparently been a factor in some instances. By far, however, the chief cause for the 50 or 75 per cent. individual is a mother of lowered resistance, of inherent weakened constitution and inability for sustained effort, which defects she transmits to her offspring.

The necessity for a great deal of attention to the physical development of those who will some day be mothers is a very urgent need.

COMMENT

There are constitutionally inferior, substandard (MacFarlane) children; thus constituted, they enter the world and thus they continue throughout perhaps a long life regardless of attempts at improvement. A trait common to all is inability to sustained effort.

Physicians and educators and all interested in the development of the young should appreciate that what often passes for indifference, indolence and inattention may be of constitutional origin and impossible of correction.

Where such is found to be the case the child's curriculum should be made to fit the child and not the child to fit any cut and dried curriculum. All such attempts mean energy wasted.

DISCUSSION

DR. BOWDITCH: I may be able to give an idea to Dr. Kerley which will help out in the education of just the type of child he describes in the earlier years of the same. I have been firmly convinced that parents do not understand their children; frequently will not try to. One can come to a better understanding of the child by open discussion in the development of a "family forum." We developed such a family forum during the last year composed of ourselves and five other families totaling twenty children. We met once a month and talked about the things that enter into the discipline of the children, about the questions of adolescence, the advantages of the public school vs. the private school, questions of agricultural work, etc. This informal discussion has sometimes led to a change in tactics in the management of our children. We have in this forum a clergyman who believes in football as a means of discipline and takes a very enthusiastic interest in the secular life. This group could be enlarged only by multiplying groups. I am convinced that in larger places larger forums could be established. There are many subjects besides those we touched upon which could educate families and bring them into closer touch with their children.

It must be very hard for a family to have a boy of 23 invalided as Dr. Kerley has described, but I cannot tell you the amount of encouragement I have had on that line. This family education is very interesting.

DR. FRIEDLANDER: In the service during the war we had young men who had to be used in some way if it was at all possible. The English developed a way of using their man power by dividing the men into six groups according to the kind of service they were suitable for. We tried to do the same thing, but were not so successful. The fact that 33 per cent. of our young men were not fitted for military service was in itself appalling. There were about 66 per cent. who were really incapable, partly because called upon to do work they were not accustomed to do. It was impossible to get men who had been clerks and stenographers to do the work that army life entailed. Some such men could only be fitted in where they could be used. I would emphasize that these conditions to which Dr. Kerley has referred do not arise at the age of 20 or 23 years but start in early life, and if we are really going to prevent these cases we must see that square pegs are not fitted into round holes, and vice versa. Most of these people are anxious to do something, but they are manifestly unable to cope with modern conditions, and I think Dr. Kerley has struck the keynote when he said we should begin early and find the occupation suited to their standards physically and mentally. The time will come when there will be cooperation between educators and physicians which will benefit the substandard individual.

DR. ADAMS: Those who served on the medical advisory boards and made the physical examination of these men can attest that the facts brought out by Dr. Kerley are correct. Some years ago I was invited to address a large audience of mothers. The subject I selected was "The Management of Other People's Children." I opened by saying, "When I see a child on the street car bite and kick and fight I am not sorry for the mother," and the women all looked horrified, but I followed it up by saying that such behavior was due to the fact that the child's training had not begun at the proper time. We should begin at the proper time and this must be early. You cannot let a boy or girl run haphazard and then send him to college and think the college can make something of him. The college may do something, but it cannot make up for the lack of early training. The man who sends his boy to college and then provides him with an automobile is doing a very wrong thing for the future of that boy. It is this species of luxury from infancy which is most harmful. We must train the parents more than the children to lay down laws for proper discipline. There must be cooperation between fathers and mothers. It does no good when the father tries to discipline a boy and the mother smooths it over. I know of one family with three sons that are not worth the powder it would take to blow them up. Two of them are married and divorced and the third drinks. When one of these boys was 12 years old his mother gave him $25 for a birthday present. He took three chorus girls to dinner with it, and his mother thought it a great joke. What can you expect from children when the parents indulge them in that way? I have known many such cases among the children of parents of wealth.

Those of us who were on the medical advisory boards saw and heard a great many things about these young men, some physically and some mentally defective. It was amusing to see how some of them tried to get off. We had a negro led in by a child. He said to the doctor, "I cannot see." "I cannot even see light." We could not find anything the matter with him. The eye-man

said he could not find out anything. We had about decided to let him go, when one said, "Wait a minute." A nickle was laid on the step, and as the negro went out he picked up the nickle. When he was brought back he said, "Boss, I could not pass dat money to save my life."

DR. EATON: Study of those cases that have a lack of something (may it not be perhaps a lack of some internal secretion?) may be interesting, and the "lack," if recognized early and supplied, might aid the constitutional disability. It may be that there is something that could be given which would enable these individuals to become more nearly normal. The cases I have seen, especially during the war time, were exceedingly pitiful. Many of them were unable to fit in anywhere, even in positions where great strain was eliminated. It seems to me that with care we ought to find a way of managing these children that Dr. Kerley has spoken of, and some others, so that we would not have the round pegs in square holes, and vice versa.

DR. GRIFFITH: Dr. Kerley's paper has interested me very much. He describes a class of people for whom there really seems to be little future, entirely without any fault of their own. The condition is clearly inherited. There is another and larger class of the unfit in which there is a distinct constitutional tendency to this condition, but in which also careful guarding during childhood and adolescence might develop individuals fitted in the future to fill a useful place in society. I refer especially to that class of overworked and overtrained schoolchildren who find it difficult to keep up with their classmates in school. This applies particularly to those of the poorer population, or those of only moderate means, who are not able to send children to a private school, and who must depend entirely on public school training. Here there are hard and fast rules insisted on which these children of inferior constitutional character cannot tolerate. In the school little allowance is made for such children. If they are able to come at all, they are obliged to attend both sessions. There is often hurry to school, a hasty going home at the noon hour, then back to the school, and out in the afternoon at an hour which in wintertime is too late for the outdoor exercise of which they are so badly in need. I do not know what can be done for these individuals. It does not seem possible for the public school to have special classes for them, and yet they need an education, and should have it. It is a matter well worthy of the consideration of all of us.

DR. BRENNEMANN: It ought to be emphasized that a certain proportion of these cases must be considered on a psychical rather than a physical basis and that we must distinguish between these two groups. There are certain children that are apparently in perfect condition physically that yet have a kind of mental inertia that is really not laziness. Such children are often shy and lack initiative and will do nothing unless forced to do so by circumstances. They are followers rather than leaders and are never fitted for executive positions. It seems to me that these cases ought to be included in this category though there is no physical abnormality of any kind that we know of.

DR. BLACKADER: Dr. Kerley has done well to bring this condition to the attention of the society. Doubtless heredity has much influence in its etiology; nevertheless, I cannot but feel that much may be done during childhood to minimize such influence. Undue strain at school, over-excitement, and a restless and dream disturbed sleep, prevent the proper nutrition of the developing nervous centers, and interfere with the development of reserve power. Any

interference with quiet restful sleep in the child is of great importance, and demands the most serious attention of the physician, and especially in the children of parents who are lacking in nervous tone from whatever cause. Avoidance of excitement and overstrain, and a well regulated dietary will also do much to correct such unfortunate hereditary influences.

DR. MILLER: The old stories always had a moral. The moral of this is, as Oliver Wendell Holmes said, "Education should begin with the great-grandparents." Another moral is that the profession has a great responsibility. We have paid too much attention to purely medical things and have neglected the moral and physical training of children and their mothers.

DR. KERLEY: A certain number of these children exist in all communities, and it should be our endeavor to have their lives so fashioned that they may develop into useful citizens. From the standpoint of prevention we shall have to begin with the grandparents, for it is an inherited weakness that produces the syndrome I have tried to outline. Another point I wish to emphasize, is that of a rather neglected field, the development of girls. We should pay particular attention to those who are to be the mothers of the future. This has been found necessary in the lower animals. Farmers and stock growers give just as much attention to the female as to the male. I feel that the growing girl is rather neglected, and to her comes the chief function of continuing a strong and vigorous race.

PRECIPITINS FOR EGG ALBUMIN IN STOOLS*

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The preparation of the stools was the same in these cases as that reported in a previous article.[1]

Anti-egg white rabbit serum of a titer of 40,000 was used. Titer equals highest dilution of egg white in salt solution in which the serum produced precipitate by contact method after one hour at room temperature.

The first group (Table 1) consisting of 103 stools from 24 cases showed three positive reactions. These stools were all from children two years or over. Two of the positive reactions occurred in the case of idiocy (Case 6). This child had a large quantity of egg in the diet since it was about the only food which she would take readily. To the other children egg was usually given in the form of ice cream and pudding only on Sunday afternoons, but occasionally during the week. The single other positive reaction that occurred in the stool of Case 4 occurred within forty-eight hours after taking this diet; but of seventeen other stools with the same relation to the diet, no positives were found.

After this initial group, it was decided to study a few cases with egg albumin given to the amount of a teaspoonful each day. For this three different types of cases were chosen. Case 1, a control case, was fed through a gastrostomy wound; the second case, a case of intestinal infantalism, and a third one of general eczema. In seventeen stools obtained from these children only one showed a doubtful reaction (Table 2).

In the third group of thirty-three cases of infants 2 years old or under, there were 221 stools. In only two of these cases was the age over 1 year. Many of them were newborn infants who had received a dilute albumin water to the amount of 10 c.c. of egg albumin to 500 c.c. of water, which was given to these infants in place of the usual boiled water. From this group 221 stools were examined with

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* From the McCormick Memorial Institute and Children's Ward of the Presbyterian Hospital.

1. Hektoen, L., and Grulee, C. G.: Am. J. Dis. Child. **18**:1 (July) 1919.

TABLE 1.—Examination of Stools of Older Children for Egg Albumin

No.	Diagnosis	Age, Years	No. of Stools	Positive Reaction
1	Chorea; myocarditis; Ludwig's angina; tonsillitis	8	28	0
2	Epilepsy	10	9	0
3	Syndactylism	5	2	0
4	Appendicitis	8	9	1
5	Chronic osteomyelitis (fibula)	9	9	0
6	Idiocy	3	14	2
7	Fractured arm	6½	2	0
8	Otitis media; mastoiditis	4	2	0
9	Osteomyelitis os calcis	8	5	0
10	Abscess of cervical glands	6	2	0
11	Diabetes mellitus	2½	1	0
12	Chorea	8	5	0
13	Skull fracture	4	1	0
14	Congenital glaucoma	2½	1	0
15	Chronic ileocolitis	2	2	0
16	Eye injury	5	2	0
17	Chorea	8	2	0
18	Otitis media	2	1	0
19	Cholecystitis	12	1	0
20	Tenoplasty for old poliomyelitis	10	1	0
21	Tuberculous meningitis	3	1	0
22	Rectal polyp	4	1	0
23	Encephalitis lethargica	2½	1	0
24	Chronic tonsillitis	7½	1	0
	Total	..	103	3

TABLE 2.—Test Cases Given One Teaspoonful of Egg Albumin per Day

No.	Diagnosis	Age, Months	No. of Stools	Positive Reaction
1	Stricture of esophagus	13	2	0
2	Intestinal infantalism	22	6	0
3	Eczema	19	9	1 (?)
	Total	..	17	1 (?)

TABLE 3.—Results of Examination of Stools of Infants

No.	Diagnosis	Age	No. of Stools	Positive Reaction
1	Prematurity	Newborn	10	0
2	Prematurity	Newborn	4	0
3	Prematurity	Newborn	1	0
4	Normal	Newborn	3	0
5	Intracranial hemorrhage	Newborn	1	0
6	Normal	Newborn	6	0
7	Normal	Newborn	3	1
8	Normal	Newborn	5	0
9	Normal	Newborn	3	0
10	Normal	Newborn	4	0
11	Normal	Newborn	2	0
12	Normal	Newborn	2	0
13	Normal	Newborn	4	0
14	Normal	Newborn	2	0
15	Normal	Newborn	1	0
16	Normal	Newborn	2	0
17	Hydrocephalus meningocele; prematurity	1 mo.	16	0
18	Prematurity	5 wks.	9	0
19	Hare lip; cleft palate	2 mos.	10	0
20	Pylorospasm	2 mos.	7	0
21	Infantile eczema	11 wks.	16	0
22	Infantile eczema	3 mos.	14	2
23	Pylorospasm	3 mos.	7	0
24	Decomposition	3 mos.	1	0
25	Pylorospasm	14 wks.	20	0
26	Rumination	3 mos.	14	1
27	Congenital syphilitic hydrocephalus	6 mos.	8	0
28	Hydrocephalus	6 mos.	9	1
29	Weight disturbance	7½ mos.	23	0
30	Rickets	1 year	5	0
31	Meningeal hemorrhage	1 year	5	0
32	Infantile eczema	21 mos.	2	0
33	Cervical cellulitis; pyelocystitis	2 years	2	0
	Total	.....	221	5

five positive reactions. One of these reactions occurred in a new-born infant who had been given the egg albuumin mentioned above. In the other three children who gave positive reactions, we know of no way to account for these, since in no instance was egg albumin present in the diet.

It would seem from these results that egg albumin is in nearly every instance completely broken down by the digestive processes in infants and children. This holds good not only for children and older infants, but also where the egg albumin is used in small quantities for the new-born as well. There is only one other possibility, and that is that the egg albumin instead of being broken down in the process of digestion is absorbed unchanged. We do not feel that specificity of the precipitin reaction for egg albumin is to any degree disproven by the fact that it was found to be positive in stools where no egg had been present in the diet. We would be inclined to attribute such reaction to the complexity of the stool.

I wish to take this opportunity to thank Dr. Ludvig Hektoen, who has been kind enough to have the precipitins prepared and the experiments done under his personal supervision; and to Dr. B. E. Bonar for the preparation of the fecal extracts.

SOME EXPERIMENTS TO DETERMINE THE PERSISTENCE OF EXTRANEOUS BACTERIA IN THE GASTRO-INTESTINAL TRACT OF GUINEA-PIGS AS INFLUENCED BY DIET *

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INTRODUCTION

It is commonly believed that the character of the bacterial flora of the gastro-intestinal tract has an important influence on health. In certain instances this is unquestioned. The implantation of sufficient numbers of certain bacteria, *B. typhosus, B. dysenteriae* or *Vibrion cholerae* in the absence of a counteracting general bodily immunity brings about the development of the infections specifically related to these organisms. So also, but possibly in a less specific way, the less well characterized gastro-intestinal disturbances of infancy and childhood are commonly supposed to be due either to the activity of particular species of bacteria or to an alteration in prevailing types of micro-organisms.

A relationship between the general type of bacterial flora prevailing in the gastro-intestinal tract and more obscure disorders, such as anemias and ill defined general intoxications, is often surmised, but scientific evidence of such an association cannot be said to have been presented convincingly. None the less, the administration of acid producing types of bacteria with the conception that they will be of benefit in limiting the activity of putrefactive types is widely practiced. A review of the literature leaves it a matter of great doubt whether the administration of the acid producing types leads to more than a most temporary change in the intestinal flora. The experiments of unbiased observers make it probable that after a short period the extraneous

* From the laboratory of the Henry Phipps Institute of the University of Pennsylvania, and the Medical Service of the Children's Hospital of Philadelphia.

bacteria are completely eliminated. Assuming that the prevalence of a type of micro-organism or of a particular species is of favorable significance for the host, it becomes a matter of considerable interest to know on what condition or circumstance the survival of the favored type is possible.

This question is closely related to another of the same general character and of equal importance, namely, the periodic variation in the prevailing type of bacteria in the respiratory tract. Not that the causes of variation in the respiratory tract are likely to be identical with those in the intestine, but the principles on which these variations take place are likely to have important common features.

The problems involved are of great interest from a biologic point of view. A complete solution of them would doubtless influence practice. What our work has to offer, however, is not a solution—merely a beginning—and a suggestion as to a method of study not previously employed. The work here presented is in a sense an extension of experiments carried out some years ago by one of us (Lewis, unpublished) in the course of which the method of study was used and some of its limitations defined. Aside from outlining a method and the conditions met with as preliminary to experimentation in this field our present paper offers one point which seems to have real interest, namely, that while *B. pyocyaneus* quickly disappears from the normal gastro-intestinal tract on a normal diet, and does not persist longer when certain obviously unfavorable diets are offered, the addition of certain favorable factors (greens) to an otherwise unsatisfactory diet does tend to favor the persistence of this organism. This may warrant the suggestion that the relationships between particular bacterial species as persistent inhabitants of the intestinal tract and particular articles of diet may be closer than has hitherto been postulated, and his idea may be worthy of further study.

REVIEW OF LITERATURE

The intestinal flora of man and other animals has been studied extensively, and has been of especial interest to the pediatrist. Not only have the types of bacteria been investigated in various intestinal disorders, but the "switching" from a predominance of one type to

another has been demonstrated.[1] Briefly stated, an excess of carbohydrate in the diet tends to favor the growth of the acid forming type of bacteria in the intestinal tract, while an excess of protein favors the growth of putrefactive organisms.

Some of Metchnikoff's pupils and followers have published investigations that attempt to support his hypothesis that the lactic acid bacillus is implanted in the digestive tract. Cohendy[2] concluded from the study of four human subjects that the *B. bulgaricus* appeared in the stool from three to five days after the first ingestion of that organism. It was found each day thereafter, and it was still present in the stool from twelve to twenty-four days after the last ingestion. In one of these patients it was revealed by an abdominal operation, which occurred during the course of the experiment, that the *B. bulgaricus* multiplied in the upper two-thirds of the colon. Results similar to these were obtained by Leva.[3] Later Cohendy experimented with thirty other subjects, including himself. In this later work he apparently did not attempt to recover the ingested organism from the stool.

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1. Hull, T. G., and Rettger, L. F.: Further Studies on the Influence of a Lactose-Containing Diet on the Intestinal Flora, J. Bacteriol. **1**:120, 1916. Penrose, C. A.: A Review of the Theories and Facts Underlying the Treatment of Diseases by Soured Milk Cultures, Maryland M. J. **58**:53, 1915. Torrey, J. C.: The Regulation of the Intestinal Flora of Dogs Through Diet, J. Med. Res. **39**:415, 1919. Herter, C. A., and Kendall, A. I.: The Influence of Dietary Alterations on the Types of Intestinal Flora, J. Biol. Chem. **7**:203, 1910. Hull, T. G., and Rettger, L. F.: The Influence of Milk and Carbohydrate Feeding on the Character of the Intestinal Flora. IV. Diet Versus Bacterial Implantation, J. Bacteriol. **2**:47, 1917. Herter, C. A.: Experimental Variation of Intestinal Flora by Changes in Diet, Internat. Beitr. z. Path. u. Ther. der Ernährungsstörungen **1**:275, 1909. Herter, C. A.: The Common Bacterial Infections of the Digestive Tract and the Intoxications Arising from Them, New York, The Macmillan Co., 1907. Porter, L.; Morris, G. B., and Meyer, K. F.: Certain Nutritional Disorders of Children Associated with a Putrefactive Intestinal Flora, Am. J. Dis. Child. **18**:254 (Sept.) 1919. Distaso, A., and Sugden, J. H.: Entero-Intoxication—Its Causes and Treatment, Biochem. J. **13**:153, 1919. Ford, W. W.; Blackfan, K. D., and Batchelor, M. B.: Some Observations on Intestinal Bacteria in Children, Am. J. Dis. Child. **14**:354 (Sept.) 1917.

2. Cohendy, M.: Essais d'acclimatation Microbienne Persistante dans la Cavité Intestinale. Delimitation du Siége Probable de cette Acclimatation, Compt. rend. Soc. Biol. **60**:364, 1906. De la Disinfection Intestinale Obtenue sans Régime Special par l'acclimatation d'un Ferment Lactique dans le Gros Intestin, Compt. rend. Soc. Biol. **60**:602, 1906.

3. Leva. J.: Zur Beurteilung der Wirkung des Lactobacillus und der Yoghurtmilch, Berl. klin. Wchnschr. **45**:922, 1908.

Belonovsky [4] conducted experiments on mice over a period of ten months. After feeding the bulgarian ferment daily to these animals, he recovered the organism in ten days by culturing the stool, and found that it persisted in the intestinal discharges for about four weeks after the return to a normal régime and the cessation of germ feeding. The author states that on examining the excrement under the microscope, there was no predominance of the bulgarian bacillus. Control mice were fed various substances, such as lactic acid, sterilized milk, bulgarian ferment killed by heat, and other organisms (*B. pyocyaneus* and *B. prodigiosus*). It was only in mice fed with *B. bulgaricus* that the total number of bacteria in the droppings was diminished. It was apparently on such evidence as this that Metchnikoff based his claim of intestinal implantation of the bulgarian bacillus, as he himself does not seem ever to have demonstrated such a phenomenon.[5]

The work of later investigators does not substantiate the theory of implantation.[6] Hull and Rettger performed one hundred and eighty individual experiments on white rats, six on other laboratory animals, and four on man. They collected and cultured the feces, but were unable to establish the *B. bulgaricus* in the intestinal tract, in spite of the ingestion of large numbers of these organisms. Herter and Kendall found that the exclusive feeding of a rhesus monkey for two weeks with milk fermented with the bulgarian bacillus failed to establish the predominance of this organism in the cecal region

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4. Belonovsky, J.: Influence du Ferment Lactique sur la Flore des Excrements des Souris, Ann. Inst. Pasteur **21**:991, 1907.

5. Metchnikoff, E., et al.: Bacteriotherapie, Vaccination, Serotherapie, J. B. Bailliere et Fils, Paris, 1909. Metchnikoff, E.: The Prolongation of Life, New York, Putnam Sons, 1908. Etudes sur la Flore Intestinale, Ann. Inst. Pasteur **27**:894, 1913. We are not concerned here with the question as to whether or not the feeding of the bacillus does good clinically. The subject under discussion is only that of the implantation of organisms in the intestinal tract.

6. Rahe, A. H.: A Study of the So-Called Implantation of the Bacillus Bulgaricus, J. Infect. Dis. **16**:210, 1915. Editorial, J. A. M. A. **73**:1844 (Dec. 13) 1919. Herter, C. A., and Kendall, A. I.: An Observation on the Fate of Bacillus Bulgaricus (in Bacillac) in the Digestive Tract of a Monkey, J. Biol. Chem. **5**:293, 1908. Luerssen, A., and Kuhn, M.: Yoghurt, die Bulgarische Saurmilch, Centralbl. f. Bakteriol. **20**:234, 1908 (Quoted by Hull and Rettger, J. Bacteriol. **2**:47, 1917. Heinemann, P. G.: Lactic Acid as an Agent to Reduce Intestinal Putrefaction, J. A. M. A. **52**:373, 1909.

or in the colon. The experiments of Rahe show that the bacillus bulgaricus is capable of an apparently limited survival in the upper intestine of the monkey. Rahe's results are shown in Table 1.

More recently the *B. acidophilus,* a normal inhabitant of the intestinal tract of man, has been introduced by mouth in order to prevent the proliferation of the proteolytic types of organisms. It may be said, however, that the proof of the implantation of organisms in the intestinal tract of man or of laboratory animals rests on incomplete evidence.

TABLE 1.—RESULTS OF FEEDING B. BULGARICUS TO MONKEY

Monkey	Fed	Period of Ingestion	Time Killed after Last Ingestion	Duodenum	Jejunum	Ileum	Cecum	Feces
1	50 tablets per day.....	13 days	24 hours	—	+	—	—	—
2	300 c.c. 48-hr. milk culture.	6 days	7 hours	+	+	+	+	+
3	300 c.c. 48-hr. milk culture.	6 days	7 hours	+	—	—	—	—

METHOD OF PROCEDURE

We have approached this subject from a somewhat different angle than previous investigators. The present study is concerned only with the attempt at implantation of an extraneous organism, the *B. pyocyaneus,* in the digestive tract of the guinea-pig. Our aim has been to study the principles governing the implantation, if such can be accomplished. If implantation should not be found possible, we may hope to find out the reasons back of this local immunity. *B. pyocyaneus* has several advantageous characteristics for a study of this kind: it is potentially pathogenic; it produces poisonous substances in culture which in its pathogenic relationships it assumes in various character, and above all it is easy of recognition.

The guinea-pig has a comparatively sterile gastro-intestinal tract. This may readily be proved by killing a guinea-pig after a twenty-four hours' fast and taking smears and cultures from the various parts of the intestinal segments. One usually finds a moderate number of organisms in the smear from the stomach; often none from the duodenal smear; a rather large number from the ileum, cecum and colon. Cultures made on agar will frequently show no growth. This negative finding is especially constant in the duodenum. Such a distribution of bacteria corresponds to that found in the intestinal tract

of man.[7] If the pig has not been in a state of fast and has a gastro-intestinal tract full of food, organisms found by smear and culture are more numerous, and different molds introduced with the food may grow in the culture. Again, if some time has elapsed between death and the taking of the smears and cultures, the organisms will be correspondingly numerous. The organisms found are gram-positive and gram-negative diplococci and bacilli, the types varying with the diet. (Cultures taken in the manner described show, of course, only the aerobic bacteria). It is possible for certain animals to live with sterile digestive tracts.[8]

The *B. pyocyaneus,* as far as we have been able to ascertain, is not a normal inhabitant of the gastro-intestinal tract of the guinea-pig. Furthermore, this organism has a low pathogenicity, for the guinea-pig can be fed in large numbers mixed with the food without causing ill effects. If fed in the manner as described it seldom enters the blood stream and causes a septicemia. It may, however, gain entrance to the circulation through the intestinal tract.[9] The *B. pyocyaneus* occasionally occurs in the digestive tract of the human apparently in the best of health. In some of our earlier experiments we introduced the *B. pyocyaneus* into the stomach of the guinea-pig by means of a small catheter used as a stomach tube. When a considerable number of organisms were introduced in this manner, the animal died exhibiting a violent gastro-enteritis and a growth of the bacillus was obtained from the heart blood. If, however, no *B. pyocyaneus* could be recovered from the gastro-intestinal canal, no evidence of gastro-enteritis was observed when the animal was killed, and the culture from the heart was negative. This method was given up, for the time being at least.

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7. Contributions to the Science of Medicine by the Pupils of William Welch, 1900, p. 543, Cushing and Livingood.

8. Nuttall, G. H. F., and Thierfelder, H.: Thierisches Leben ohne Bakterien im Verdauungskanal, Ztschr. f. Physiol. Chem. **21**:109, 1895; **22**:62, 1896; **23**:231, 1897. Wolmann, E.: Sur l'elevage des Mouches Steriles, Ann. Inst. Pasteur **25**:79, 1911. Cohendy, M.: Experiences sur la Vie sans Microbe, Ann. Inst. Pasteur **26**:106, 1912. Bakteriologische Darmuntersuchungen, Skand. Arch. f. Physiol. **16**:249, 1904. Freeman, L.: Chronic General Infection with Bacillus Pyocyaneus, Tr. Am. Surg. Assn. **34**:113, 1916.

9. Freeman, L.: Chronic General Infection with the *Bacillus Pyocyaneus,* Tr. Am. Surg. A. **34**:113, 1916.

TECHNIC

With the exception of these experiments the technic of the study was as follows: Guinea-pigs that were offered various diets were fed the *B. pyocyaneus* for variable lengths of time. Later, in order to make the experiments uniform, all the pigs were fed the germ for three days. A fresh twenty-four hour culture of a strain of the *B. pyocyaneus* which produced a brilliant green color was washed from an agar slant with about 5 c.c. of physiologic sodium chlorid solution and thoroughly mixed with the day's supply of food for the pig. On cessation of the feeding of *B. pyocyaneus,* nourishment of the pig continued with the various diets unmixed with the organism. At variable lengths of time the pigs were killed and cultures made on agar from the heart blood, the stomach, the duodenum, the ileum, the cecum and the colon. If the pig died the same cultures were made. These cultures were incubated for twenty-four hours, and after that kept at room temperature. No tube was declared negative for the *B. pyocyaneus* until at least five days had elapsed without evidence of green pigmentation. After having first ascertained that it was the *B. pyocyaneus* with which we were working, an appearance of the green pigment was considered sufficient evidence of the presence of that organism in the cultures. The + marks in the charts indicate the amount of green pigmentation appearing in the agar, + a small amount of the color; ++ a larger amount, coloring about half the agar slant; +++ when all the agar was permeated with the pigment.

A series of experiments was first undertaken to ascertain whether or not the *B. pyocyaneus* would grow in the gastro-intestinal tract of the guinea-pig, and whether or not diet had any effect on such growth. Previous to the feeding of the *B. pyocyaneus* mixed with the food, the pigs had been fed on their regular diet which consisted of oats and bread mixed with water, hay, and green stuff twice a week. Of the fourteen pigs used, three were continued on their regular diet and the *B. pyocyaneus* was mixed with the oats, bread and water for two days. *Bacillus pyocyaneus* was recovered from the cecum of two of these pigs when killed one or two days later, but not from the pig killed four days later. The remaining pigs in this series were kept on their regular diets until the day on which they received their first *B. pyocyaneus* feeding mixed with their new diets. They did not take the abnormal diet well, and there is, therefore, some doubt as to the amount of germ ingested. However, in three of these pigs

the *B. pyocyaneus* was recovered either from the ileum or cecum or both, when killed two days after having been previously fed *B. pyocyaneus* for two days. These three pigs had been fed on hay and water, milk and water, and crackers and water respectively. Other pigs in this series had been nourished on crackers and milk, bread and milk, bread and water, oats and water. From the pigs thus fed *B. pyocyaneus* could not be recovered when they were killed two days after the cessation of a two day period during which that organism had been administered with the food.

In order to find out whether the length of time during which the *B. pyocyaneus* was fed had any effect on its persistence in the digestive tract, several pigs were fed with the organism mixed with their regular diet for variable lengths of time (from three to fourteen days) and then killed at intervals of from two to eleven days. In none of these pigs was the *B. pyocyaneus* recovered when cultures were taken from the different parts of their intestinal tract and stomach (Table 2).

TABLE 2.—RESULTS IN PIGS FED ON NORMAL DIET OF OATS, HAY, BREAD AND GREEN STUFF. B. PYOCYANEUS MIXED WITH THIS NORMAL DIET FOR VARIABLE LENGTHS OF TIME. NORMAL DIET CONTINUED UNTIL PIGS WERE KILLED OR DIED

No. Days Pigs Fed	Killed or Died	Day Killed or Died	Heart Culture	Stomach Culture	Duodenum Culture	Ileum Culture	Cecum Culture	Colon Culture
2	K	1	.....	0	0	0	+	
2	K	2	.....	0	0	.....	+	
2	K	4	.....	0	0	0	0	
3	K	4	.....	0	0	0	0	0
3	K	5	.....	0	0	0	0	
3	K	6	N.G.—0	0	0	0	0	0
3	K	7	.....	0	0	0	0	0
3	K	8	N.G.—0	0	0	0	0	0
3	K	9	N.G.—0	0	0	0	0	0
3	K	11	N.G.—0	0	0	0	0	
7	K	3	.....	0	0	.....	0	
14	K	2	N.G.—0	0	0	0	0	0

Day killed or died, i.e., day after last ingestion of pyocyaneus. In the columns showing the results of culture, a blank indicates that no culture was taken; O indicates that there was no growth of pyocyaneus; N.G. indicates that there was no growth or any type of organism; + indicates a growth of pyocyaneus.

The thought presents itself as to whether or not much of the pyocyaneus is ingested when the organism is mixed with the regular diet of oats, bread and water, hay and green stuff. It will be remembered that in eating the whole oat the pig cracks open the outer covering of the oat kernel, discards this covering and eats the softer center.

By using rolled or crushed oats the culture of *B. pyocyaneus* can be mixed thoroughly with the food. Accordingly, four pigs were fed in this manner. First, they were given a two-day diet of rolled oats without pyocyaneus. This was to accustom them to their diet, or at least to assure sufficient hunger so that during the three following days in which the *B. pyocyaneus* was fed a considerable amount of the germ-mixed food would be ingested. On discontinuing the feeding of the organism, the regular diet was instituted. The *B. pyocyaneus* was not recovered from any of the pigs of this series when killed at intervals of from five to eleven days later. On the normal diet, *B. pyocyaneus* does not, then, persist in the digestive canal.

Several other experiments were carried out, the details of which need not be given. Briefly, they consisted in feeding series of pigs on a simple died of oat kernels and water. In some of these series the attempt was made to assure the ingestion of the bacillus by mixing it with oats and water eighteen hours or less before feeding. It was found that the organism did not always live under such circumstances.

In order to remove doubt as to whether the *B. pyocyaneus* was ingested because of the failure of the pigs to eat an abnormal diet, such as rolled oats, a number of pigs were fed *B. pyocyaneus* only after they had been previously fed on rolled oats alone for a week. Over 50 per cent. of the fourteen pigs in this series died.[10] We believe that it is seldom, if ever, that guinea-pigs die as the result of the ingestion of *B. pyocyaneus* when mixed with the food, but that death is due rather to the lack of essential elements in the limited diet. It will be seen later that the addition of green stuff to the rolled oats partly overcame this difficulty, and that only four of fifteen pigs (about 25 per cent.) died. It is probable from the necropsy findings and the cultures that at least two of these four pigs died from an infection with an organism of the paratyphoid group. *B. pyocyaneus* was recovered from the gastro-intestinal tract of nine of the fourteen pigs (Table 3). Three of these nine pigs died two days after the cessation of pyocyaneus feeding; three died three days after; one died four days after; one was killed seven days after and one was killed nine days after. Of the five pigs in which the *B. pyocyaneus* was not recovered one died at the end of the first day after the attempt to feed *B. pyocyaneus* and this pig was apparently sick at the time with

10. Three control pigs that were fed simply on rolled oats and water without at any time the admixture of *B. pyocyaneus* died at eight, eight, and fifteen days, respectively, after the institution of the régime.

an infection by an organism of the paratyphoid group and did not eat the food mixed with the *B. pyocyaneus*. Of the other four, one was killed at the end of five days, one at seven days and ten at the end of nine days.

TABLE 3.—PIGS FED ROLLED OATS FOR ONE WEEK; THEN ROLLED OATS PLUS B. PYOCYANEUS FOR FROM ONE TO THREE DAYS. A DIET OF ROLLED OATS WAS THEN CONTINUED. THREE CONTROLS NOT FED B. PYOCYANEUS DIED AT EIGHT, EIGHT AND FIFTEEN DAYS, RESPECTIVELY

No. Days Pyo. Fed	Killed or Died	Day Killed or Died	Heart Culture	Stomach Culture	Duodenum Culture	Ileum Culture	Cecum Culture	Colon Culture
3	D	2	+++	+++	.....	.....	++	
3	D	2	N.G.—0	+++	.....	.....	+++	
3	D	3	N.G.—0	0	0	.....	++	0
3	K	5	N.G.—0	0	0	.....	0	0
3	K	7	N.G.—0	+++	++	0	++	+
1	D	1	N.G.—0	0	0	0	0	0
2	D	2	N.G.—0	++	++	++	+++	++
3	D	3	+++	+++	N.G.—0	+++	+++	+++
2	D	4	N.G.—0	++	++	++	0	
3	D	3	N.G.—0	+	0	++	+++	0
2	K	7	.....	0	N.G.—0	0	0	N.G.—0
2	K	9	.....	0	0	.....	0	0
3	K	9	.....	+	++	.....	0	0
3	K	9	.....	0	0	0	0	0

\+ Indicates a slight growth of pyocyaneus.
++ Indicates a more active growth.
+++ Indicates a large amount of growth.

In the next experiment a small amount of green stuff was added each day to the rolled oats diet. *B. pyocyaneus* was recovered in all at the end of seven days after the cessation of *B. pyocyaneus* feeding, one was killed nine days after feeding ceased and one was killed thirteen days after feeding ceased. Of the pigs in which *B. pyocyaneus* was recovered, two died the first day after the cessation of pyocyaneus feeding; one was killed after five days; one was killed and one died after seven days; one was killed at eight days; three were killed at nine days; one was killed at ten days; one was killed at eleven days and one was killed at twelve days (Table 4).

Ten pigs were now fed rolled oats and butter for five days, then *B. pyocyaneus* was mixed with this food for three days and the rolled oats and butter diet continued thereafter. In all of this series *B. pyocyaneus* was recovered from the digestive tract when the pigs were killed or died from three to thirteen days following the cessation of germ feeding. Five pigs died at three, four, seven, nine and ten days, respectively, and five were killed at five, five, seven, eleven and thirteen days respectively (Table 5).

TABLE 4.—PIGS FED ROLLED OATS PLUS GREEN STUFF FOR FIVE DAYS; THEN ROLLED OATS PLUS GREEN STUFF PLUS B. PYOCYANEUS FOR FROM TWO TO THREE DAYS. A DIET OF ROLLED OATS AND GREEN STUFF THEN CONTINUED

No. Days Pyo. Fed	Killed or Died	Day Killed or Died	Heart Culture	Stomach Culture	Duodenum Culture	Ileum Culture	Cecum Culture	Colon Culture
2	D	1	N.G.—0	+++	+++	.....	+++	+++
2	D	1	0	+++	+++	+++	+++	0
3	D	7	N.G.—0	+++	0	++	+++	+
3	D	10	N.G.—0	+	0	.....	++	++
3	K	5	+	0	N.G.—0	++	+	0
3	K	7	N.G.—0	0	0	0	0	
3	K	7	N.G.—0	N.G.—0	.....	0	+	N.G.—0
3	K	9	.....	0	0	0	+++	0
3	K	9	N.G.—0	+++	++	0	0	0
3	K	9	N.G.—0	0	0	0	+	
3	K	9	N.G.—0	0	0	0	0	0
3	K	9	N.G.—0	0	0	0	++	0
3	K	10	N.G.—0	+	0	.....	++	++
3	K	11	N.G.—0	0	0	0	++	0
3	K	12	N.G.—0	0	N.G.—0	0	+	0
3	K	13	N.G.—0	0	N.G.—0	0	+	0

TABLE 5.—PIGS FED ROLLED OATS PLUS BUTTER FOR FIVE DAYS; THEN ROLLED OATS PLUS BUTTER PLUS B. PYOCYANEUS FOR THREE DAYS. A DIET OF ROLLED OATS AND BUTTER WAS THEN CONTINUED

Killed or Died	Day Killed or Died	Heart Culture	Stomach Culture	Duodenum Culture	Ileum Culture	Cecum Culture	Colon Culture
D	3	N.G.—0	0	+	+++	+++	0
D	4	N.G.—0	0	0	.....	+++	N.G.—0
K	5	N.G.—0	N.G.—0	N.G.—0	.....	++	0
K	5	0	0	0	++	+++	+++
D	7	N.G.—0	++	++	0	++	++
K	7	0	0	0	N.G.—0	+	0
D	9	N.G.—0	+	+++	++	++	0
D	9	N.G.—0	++	++	0	+	0
K	11	N.G.—0	0	N.G.—0	.....	+++	0
K	13	N.G.—0	+	++	+	+	++

SUMMARY AND CONCLUSIONS

Bacillus pyocyaneus when fed to guinea-pigs nourished on a diet of oats, hay, bread and green stuff (the normal diet in this laboratory) usually disappears from the gastro-intestinal tract within three days. When oat meal is given as a sole article of diet, the *B. pyocyaneus* has been found at seven and nine days after the last administration. The addition of a small amount of green stuff, or of a certain amount of butter to the oatmeal diet, has apparently prolonged the period of persistence of the bacterium: *B. pyocyaneus* on these slightly amplified diets has been found to persist about two weeks with considerable

regularity. This increased persistence is probably apparent only. The animals on a strict oatmeal diet do not live long enough to enable a complete experiment to be carried out much beyond eight or ten days.

Bacillus pyocyaneus could not be recovered from the digestive canal in any case more than sixteen days after the cessation of its ingestion by mouth. Judged by the amount of pigment produced in the culture, the number of surviving bacteria became progressively less the longer the time interval following the cessation of its ingestion by the pig. *B. pyocyaneus* persisted more readily in the cecum than in other parts of the digestive tract, next in the stomach, although it was often found on culturing the duodenum, ileum and colon. This was true whether the pigs were killed soon after the cessation of *B. pyocyaneus* feeding or only after a longer interval.

It is probable, on the basis of these experiments, that there is an effect of dietary deficiency which consists in the depression of a normal mechanism controlling the implantation of extraneous bacteria in the intestinal tract.

LACTIC ACID MILK

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AND

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BUFFALO

The motive of our study of lactic acid milk was to investigate the reasons for the variations in this preparation of milk, and to devise a means, if possible, to prevent their occurrence. Furthermore, we desired to devise a simple method of preparation that would always insure a uniform product, and one that would remain unchanged.

Particularly when made through the fermentative action of the Bulgarian bacillus has lactic acid milk been considered efficient to inhibit the action of putrefactive germs in the intestinal canal, and hence to lessen the absorption of their putrefactive toxic products. To the Bulgarian bacillus was given most of the credit for this beneficial result, but according to Herter, Bryce, Mendell, Bastedo and others, the Bulgarian bacillus has no real value in this direction. If this is true, how has lactic acid milk a therapeutic effect?

To aid digestion, hydrochloric acid is the acid of our choice, but it has been stated other acids can be substituted for it, and that they will produce more or less good results. Consequently, if the fermentative action of the special bacillus, the Bulgarian bacillus, is theoretically correct but practically doubtful, the beneficial results from lactic acid milk must largely be due to the acid. If the results do depend on the acid, they must follow because the acid stimulates the gastro-intestinal function, through raising the acidity of the stomach to a point where it not only aids gastric digestion, but later stimulates the digestive secretions of the upper intestines, when it is poured into the duodenum.

But it is questioned if acids other than hydrochloric acid are aids to digestion. Often the presence of lactic acid in an adult gastric analysis indicates a hypochlorhydria, and if hydrocholric acid is administered, it prevents the formation of lactic acid, which under the circumstances is considered an abnormal acid, an acid disturbing rather

than aiding digestion. If this theory, as applied to the adult stomach, is correct, it is not the lactic acid itself which gives lactic acid milk its therapeutic effect.

The question then arises, How does it aid? According to the newer ideas of the gastro-enterologists, it is Meltzer's law of "contrary innervation" that has so much to do with the gastro-intestinal functions. It is agreed according to this law that whatever increases the amplifications of the waves of peristalsis will, through this increased relaxation and contraction, increase the function of the gastro-intestinal canal.

Following this law lactic acid may favor the amplification of peristalsis and thereby improve function. Practically it does seem especially efficient in the very class of cases of infants in which we desire to use lactic acid milk, that is, in those cases which are physically undertone, those with dilated stomachs due to a relaxed musculature.

Lactic acid milk differs from ordinary sour or spoiled milk, because it is a sour uncontaminated, sterile milk.

At the Children's Hospital for the last eight months we have been using lactic acid milks in the different feeding cases, and have been very much pleased with our results. We are inclined to believe that our results are as good, if not better, than with the much-lauded protein milk.

Protein milk is advised especially for six main reasons, e. g., the high protein with its high calcium, the full fat, the low milk sugar, the low soluble salts, the fine curd during digestion and the concentrated food.

If our contention is true, it is the lactic acid in the protein milk which is the stimulator of digestion, both gastric and intestinal, and the sterilizer of the intestinal contents.

With our method of mixing we get four of the points of advantage which are emphasized in protein milk. We can secure a relatively high protein, a full fat, the fine curd during digestion and the concentrated food. The amount of milk sugar, which is nearly the same as in sweet cow's milk, may be considered a disadvantage. But this is not a major disadvantage because lactic acid milks contain only 1.5 per cent. more milk sugar than does protein milk.

In protein milk, great stress is laid on the decreased salt content. In comparison lactic acid milk does contain nearly twice as much of the soluble salts as does protein milk and less of the insoluble salts, the calcium and magnesium.

In the few cases where we must use a low soluble mineral element, and a high insoluble mineral element protein milk is without doubt the better food, but the accuracy of the needs of the infant for this chemical relationship of the soluble and insoluble salts has not been demonstrated without question.

In the first place, we use two kinds of lactic acid milk: one made of skimmed milk and the other of whole milk. This makes the formulae very flexible as regards the use of fat, the tolerance for which is so commonly broken in this class of case. We are apt to start with the skimmed lactic acid milk, and we work it up to the desired ratio with its diluent, or as high as it can be well borne. As the child's digestive tolerance permits, we replace the skimmed lactic acid milk by the whole lactic acid milk.

We find Marriott's statement true that an unexpectedly high ratio of lactic acid milk, especially if skimmed, can be used.

With this high ratio, we secure a fairly high protein which is considered so essential.

In order to make the formula smooth, we have mixed the lactic acid milks with barley water. The resulting mixture has an attractive appearance, and we find the barley water to be a great aid in holding the mixture in even suspension. We make the barley water of a strength of from 0.5 to 0.75 per cent.

The great difficulty with any lactic acid preparation is the control of the acidity as the buttermilk ages. If the acidity is too low and if the milk is not clotted in fine curds, it clumps into a large mass when boiled, even though stirred. If the acidity is too high, the infants either refuse or reject it.

But the difficulty is how to get that acidity and keep it. We have worked out two simple methods which we hope time will prove to be satisfactory and successful.

In both the methods we boil the milk first so as to have an uncontaminated fermentation.

The first method is to warm the milk, that has been boiled and then cultured, and put it away, either in a fireless cooker or the ordinary child's ice box, so frequently found in the household. If the cultured milk is put away in the evening at 85 F., in the morning it will be found to have undergone a proper fermentation with an acidity of about 70 or 90. To check further fermentatiaon we put it on ice or, preferably, rapidly bring it to a boil. I mention rapid boiling, because

slow boiling lengthens the period in which the warmth is sufficient to favor fermentation and hence the increase of acidity. During this boiling active stirring with a Dover egg beater is essential to keep the curds fine and prevent clumping.

This boiling renders the fermenting Bulgarian bacillus inert, and leaves a milk sour but sterile; a milk which is very different from a sour milk spoiled by various ferments and a milk that is probably as efficient as if the bulgarian bacillus were active.

The second method is still simpler.

It is a well-known fact that the fermentation of lactic acid milks continues up to a certain point of fermentation, that is, of acidity. At about 60, as measured by decinormal sodium hydrate solution, spontaneous fine clotting occurs. At about 170 or 190, the acidity destroys or renders inactive the fermenting bacillus and the process consequently of itself ceases.

We have taken the milks, either skimmed or whole, and in the morning added the ferment (1 ounce of ferment to 31 ounces of milk), and stood them away in a warm place till a convenient time the next morning. Knowing by numerous tests that the acidity has reached about 170 to 190 by that time, we dilute the skimmed or whole lactic acid milk with an equal amount of skimmed or whole sweet milk, that has been boiled, and we have the desired acidity of about 75 to 90. Because the acidity is above 60, there occurs a spontaneous fine clotting of the added sweet milks with a resulting homogeneous smooth clotted mixture. This mixture of lactic acid and sweet milks is then boiled or not, as we desire. It is then further modified, as the case demands, and put away on ice. It keeps nicely, changing very little in the following twenty-four hours, the change being much less if boiled a second time.

This is surely a simple method that can be carried out even in the household of the ignorant. It requires merely the making of a certain amount of whole or skimmed lactic acid milk, to which can be added an equal amount or more of whole or skimmed boiled sweet milk.

The small clots, which are formed during the process of fermentation, are flocculent in character and are very easily digested. Should the infant reject the lactic acid milk of correct acidity, the curds are small and soft and show evidence of prompt digestion.

To supply the carbohydrate needs we have added Karo or corn syrup: first, because of its contained variety of sugars, and second, because it is cheap. We have had an unopened can cultured and found it germ free.

Our series of cases tested on lactic acid milks has amounted to only about twenty-five, and I may consequently be presuming to make a report on such a small number.

Given a mixture of the proper acidity, we find the infants very quickly seem to like it, and furthermore, those with rebellious stomachs retain it nicely.

The effect on the stools is marked and quickly obtained. The foul putrefactive odor, so common in this class of hospital case, promptly ceases, and the stools become even, smooth and of good color.

The infants seem rapidly to become less toxic, as is shown by the disappearance of various signs and symptoms.

1. Their appetites improve, and they take the formula well and are apt to retain it.

2. They soon lose their ashy gray color. Their mucous membrane, especially of the lips, shows a decided betterment in color. This occurs before the gain in weight has been marked.

3. Their temperature becomes more stable and an early monotherapy occurs.

4. They soon become less fretful; in other words, are more happy.

5. Their sugar tolerance seems less easily broken, and gas formation is less apt to complicate the condition.

6. The loss of weight, or stationary weight, is soon apt to be overcome by a substantial weekly gain, and caloric feeding seems easier to reach.

The age of the infant seems to make very little difference with lactic acid milks. Finkelstein does not advise protein milk before 3 months of age, though this rule is not inflexible. But we have used lactic acid milks in the very young with as good results as with older infants. As an example, one of our patients was a premature infant of seven months' gestation, weighing 4 pounds at birth. At the end of its first month it weighed 5 pounds. It was started on its second day of life with a one-half skimmed lactic acid milk. This was

gradually raised to a two-thirds mixture of lactic acid milk, which was made of one-half skimmed lactic acid milk and one-half whole lactic acid milk. This is approximately a 2 per cent. fat mixture.

The therapeutic effects of lactic acid milk or buttermilk are too often only superficially understood. The curds formed from it are small and easily cared for. The acidity seems to stimulate both the gastric and intestinal function, and the sterilization of the protein fermentation of the intestinal canal is marked. This change of intestinal state markedly lessens the absorption of toxic products, and the whole process of metabolism is hence beneficially affected.

DISCUSSION

DR. HOOBLER: I have used lactic acid milk unboiled and I would like to know why Dr. Sherman finds it necessary to boil it and kill the lactic acid bacilli.

DR. SHERMAN: It was boiled to control the acidity, for the acid would not increase if the Bulgarian bacilli were rendered inert.

SOME OBSERVATIONS ON THE ROLE OF CERTAIN ANAEROBES IN THE INTESTINAL FLORA OF INFANTS

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SAN FRANCISCO

That the bacterial flora of the normal stools of healthy infants is characteristic in the kinds and proportions of the contained organisms is a fact well established by the researches of Escherich, Herter, Tobler, Kendall and others. Recently the studies of Kendall, Torrey and Karl Meyer have extended our knowledge in this field. Meyer has shown that the stool of the infant in normal health contains a variety of bacteria, part of them carbohydrate splitters, part of them protein hydrolyzers, and that these exist in such proportions that neither can assert a predominance.

Last year I read a paper before this Society incorporating some of Karl Meyer's researches on the subject. Besides the bacteriologic aspects, certain clinical features which accompany deviations of this normal intestinal floral balance were also discussed. The observation was made and recorded that in certain patients with alimentary intoxication, protein splitting organisms predominated in the stools and that with an amelioration of their symptoms there was a change in the proportion between the protein splitting and carbohydrate feeding bacteria; the protein splitters were much diminished in number and they were in great part replaced by carbohydrate avid organisms, with the result that a normal floral balance was again approximated.

On the other hand, other definite clinical entities were found in which the carbohydrate splitting organisms were present in excess in the stools. Individuals so affected presented an entirely different clinical picture, and when their abnormal symptoms disappeared it was found that protein splitting organisms had replaced many of the bacteria of saccharolytic type and the intestinal flora had again adjusted itself so that its cultural reactions were the same as those given by stools derived from a healthy infant.

The limitation of protein and the use of a feeding rich in carbohydrates usually bring about an unbalance of the two types of bacteria

because saccharolytic organisms are encouraged to grow. The first symptoms that follow this unbalance are identical with the clinical appearance of what is usually known as a sugar diarrhea; that is to say, the stools are increased in frequency and in quantity; they are green in color, acid in reaction, and contain a great deal of mucus, while the odor is characteristically sour with the smell of lactic acid. As the condition persists, the stools become more watery, more acid, more excoriating and more frequent; the symptoms of dehydration supervene, and an alimentary intoxication with acidosis appears. High protein feeding, by choice, protein milk, with limitation of carbohydrates is often followed by a disappearance of the symptoms unless anhydremia has persisted long enough to produce an intoxication. After milk protein feeding, the bacteria of such stool may be found to approach the normal in their proportion between their contained proteolytic and saccharolytic types.

On the other hand, there are many cases of diarrhea, some with putrid or mousy odored stools, a few even odorless, in which the evacuations are brown, lacking in homogeneity, alkaline or neutral in reaction, and passed with but moderate frequency. The use of protein-milk as a therapeutic measure in the treatment of such patients is invariably followed by an increase in the diarrhea and damage to the individual, while the use of a high carbohydrate feeding, malt soup or cereal, together with a limitation of protein intake, is successful in their treatment. A bacteriologic examination of the stools made at the height of these seizures shows great preponderance of protein splitters. Further investigation after the successful use of malt soup or cereal feeding reveals an increase in the saccharolytic organisms and later, a balanced flora.

In private practice and in the clinics of the San Francisco Children's Hospital and the University of California Hospital, it has been found a simple matter in most cases to remedy these lesser alimentary intoxications and diarrheas by the institution of appropriate dietetic measures. In deciding what particular measures are appropriate in a given case, the clinician must be guided by a consideration of both the clinical and bacteriologic facts just outlined.

In the work of the past three years certain refractory cases have been encountered. Superficially, these are like the ordinary instances of alimentary intestinal intoxication, but cases of this sort are either quite unaffected by the dietetic measures usually effective in relieving

such intoxication or under these they develop new unexpected and perplexing symptoms. So far as our limited experience with this type of case has gone, it seems that they may be divided into three groups.

1. Those in which the flora is difficult to change. That is to say, certain patients have shown a predominance of the symptoms of proteolysis, but persistent feeding of carbohydrates has not been followed by an amelioration of the symptoms or by an adequate shift in the type of bacteria in the stools.

2. Those in which the bacteria change very rapidly but in which the change is not accompanied by any great alteration in the clinical picture.

3. Those in which the predominant types of bacteria alter but in which apparently the changed diet creates another set of clinical symptoms damaging to the patient.

Of the first group are cases that present a clinical aspect characterized by colic, distress after eating, abdominal distention and flatulence so great that it interferes with sleep. This is a condition frequent during the first two years of life. Often these children are subject to mild diarrhea, although some times they are obstinately constipated. At times this syndrome is complicated by the evidences of an alimentary intoxication which in its dominant features is similar to the alimentary intoxication usually associated with an excessive proteolytic flora. A microscopic and cultural examination of the stools of such patients reveals that besides the protelytic and saccharolytic flora there are always great numbers of spore bearing anaerobes present. In many instances these are *B. welchii* and, in a smaller proportion, allied bacteria. It is probable that there are other unidentified anaerobic organisms which are predominant in the intestines of children who show symptoms of alimentary intoxication. Our knowledge of the anaerobes inhabiting the intestine is limited; it is especially limited in regard to certain less common anaerobes which are sometimes found in quantity in the intestinal tract.

In the Hooper Research Laboratories during the past few years progress has been made in developing methods for the study of anaerobes in general, especially those forms found in the stool, and it is my hope that at future meetings I will be able to present facts that may throw light on their possible relation to obscure alimentary intoxications of children. For the present I can deal only with a few phases of the activities of the Welch bacillus and a few allied spore

bearers. These are facultative organisms and as such they have the power under certain circumstances to produce protein split products which may be the cause of intoxicative symptoms. On the other hand, in other states of their development they attack carbohydrates with great avidity to produce large quantities of gas, and some strains apparently develop toxins as well. The metabolic products of a few of these strains are exceedingly poisonous.

The Welch bacillus, as isolated from the feces, is a spore bearing, facultative feeder, strictly anaerobic. It does not germinate in the presence of acid. It may exist in one of two stages:

1. A sporulating, resting stage which it assumes when the environment is unfavorable.

2. A vegetating stage during which it grows vigorously, reproducing its successive generations with great rapidity.

In the resting or sporulating stage, the organism falls into a physiologically inert condition, but the potential for the future vegetative stage is present in the spore which is highly resistant to all physical and chemical influences, especially to heat and to high acidity; but apparently when the organism begins to pass from the sporulating to the vegetative stage it is vulnerable to lactic acid. However, once the vegetative stage is well established, the organism becomes greedy for lactose and produces a great deal of gas as well as butyric acid while it is utilizing this sugar and, if the strain of Welchii happens to be a toxin producer, probably much toxin as well. The Welchii multiply rapidly and die rapidly in the presence of lactose unless the aciduric organisms have had an opportunity to establish themselves and develop a high degree of lactic acidity in the intestinal content before the anaerobes have passed into the actively vegetative stage. If this transitional period in their lives coincides with that in which the concomitant aciduric organisms are producing large quantities of lactic acid the Welchii are unable to tolerate their environment and rapidly die and disappear.

Curiously enough, while these organisms are vulnerable to lactic acid, they seem resistant to butyric acid. This fact is true not only of these anerobes but of some aerobes as well. Butyric acid production is a function of proteolysis by certain types of protein splitting bacteria. As a result, it is very easy to be misled by the clinical appearances of the stools. A definite proportion of acid stools are distinctly proteolytic. These stools have a butyric, acetic or formic odor; they

are green in color and are permeated with bubbles. It is a safe clinical conclusion to draw that a proportion of bubbly, diarrheic stools with a butyric acid odor are primarily proteolytic and not saccharolytic, and that the clinical symptoms of the case will respond better to a carbohydrate than to a high protein feeding, provided the number of functioning carbohydrate splitting organisms is first reduced by purgation and carbohydrate starvation.

Frequently these facultative organisms are encountered as part of the flora in cases in which proteolyzers are predominant and sometimes, when an attempt is made to feed carbohydrates in quantity in order to encourage aciduric bacteria, Welchii attack the sugars and dextrins present, producing so much gas and such abdominal distention that it becomes necessary temporarily to withdraw carbohydrates. However, most often when a train of events takes place there is a simple expedient at hand. This expedient depends on the fact that only in the resting stage does the anaerobe have the power to tolerate the acid produced by its own growth on carbohydrates. These spore bearers can be brought into the vegetative stage in which they cannot tolerate acid. This is best done by giving the patient a preliminary purge and placing him for twenty-four hours on an egg and water feeding which is a semistarvation diet high in protein. This twenty-four hours' feeding is then followed by one or two days' diet of protein-milk without added carbohydrate, and this in turn by a further purge. After this, an immediate change in the type of feeding can usually be made with good effect, and for the next few days lactose or lactose cream mixtures are given. As a rule, this procedure is followed by the disappearance of the spore bearers, or at least by their maintenance in the vegetating stage where they produce less gas and are easily vulnerable to lactic acid. Clinically, this method is very effective in overcoming symptoms of colic, flatulence and restlessness at night which occur so often during the first and second years of life in both breast and artificially fed babies, and usually it is equally effective as an adjuvant in those cases of acute and subacute alimentary intoxications which show a dominant proteolytic flora but in which it has been found impossible to use high carbohydrate feeding because excessive flatulence and distention have appeared coincident with the use of large amounts of lactose in the diet.

The rationale of this treatment may be divided into four steps.

1. By purgation, to reduce the number of all forms of bacteria that are inhabiting the gut.

2. By means of starvation and subsequent carbohydrate deprivation to induce spore bearers to assume the sporulating stage.

3. By further purge to reduce the number of these sporulating organisms as well as of other bacteria present.

4. Later by means of protein deprivations and high carbohydrate diet to encourage the growth of aciduring organisms. It is well established that *B. welchii* at least and probably several other spore bearing organisms are unable to return to the vegetating stage in the presence of a vigorous aciduric intestinal flora.

The advantages gained by the treatment are:

1. Gas production, flatulence, distention and colic are minimized or abolished.

2. The difficulty of swinging a proteolytic flora to normal balance because of the presence of many facultative spore bearers in the gut is overcome.

3. The possibility of any intoxication from toxic strains of *B. welchii* which may be present in the intestinal flora is done away with.

In one of the cases on which this paper is based, the flora were exceedingly persistent. Even in the presence of a very high degree of acidity, the child showed little amelioration in the symptoms of alimentary intoxication. From the stools of this patient a strain of acid tolerant colon bacillus was isolated. The clinical course of this case seems to indicate that even in the presence of large amounts of acid there are colon bacilli and probably other organisms which can break up protein with the production of deleterious absorbable split products.

The colon bacilli in this case were divisible into two strains.

1. Acid resistant.

2. Acid labile.

In this particular instance, the acid labile group largely outnumbered the acid resistant but the latter produced abdominal distention in the intestine and large quantities of gas and indol. They were unaffected in any way by the presence of lactic acid in a concentration p_H 4.4. Growing on a lactose medium, they themselves showed an end point 4.8. It was demonstrated that this strain increased the

p_H in the test tube by producing an unidentified fatty acid. There is some reason to believe that those cases in which the shift of the flora takes place only after very long periods of time may be due to the persistence of this or of allied types of colon bacilli. In cases that we have studied, it has taken as long as six months to effect shifting.

In those cases in which the flora respond by the expected change to an alteration in the character of the diet but in which the diarrhea or symptoms of intoxication persist, there is usually evidence that the pancreas has been damaged and that the patients are suffering from a mild or severe pancreatic insufficiency. The observation has been made that injections of histamin and the absorption of this substance or of allied protein split products from the intestinal loops of experimental dogs bring about pancreatic damage with temporary insufficiency of that gland. We are not prepared at the present time to deal with the various problems that exist in this particular field of pathology. Neither have we the experimental or bacteriologic data that will enable us to understand the behavior of the intestinal flora which have been observed in a clinical study of giant colon, nor are we entirely clear about all the causes that render the stool flora resistant to dietetic influences in those cases which show definite pancreatic insufficiency.

What information we have been able to obtain since our last communication refers entirely to the group of intestinal toxemias in which the abnormal stool bacteria are resistant to dietetic measures usually adequate to produce a change in the flora.

In conclusion it may be said that in the course of this study, very rarely, certain specialized strains of colon bacilli have been encountered. These are highly facultative and are excessively acid resistant; so far no effective method has been devised for overcoming their interference when they are present in the stools.

On the other hand, investigation of the evacuation of the majority of patients whose stools show a similar resistance to change in floral balance reveals the presence of unusual numbers of spore bearing organisms, most often anaerobes, usually Welchii, which interfere by virtue of their facultative powers. This facultative function enables them to utilize any pabulum present. Because of their power while in the active stage to utilize carbohydrates, they are especially apt to interfere when an attempt is made to shift a proteolytic flora by feeding the patient a high sugar diet. However, by the method suggested here this interference can be overcome and the disappearance of these spore bearing organisms from the stools insured.

THE MEDICAL SUPERVISION OF THE BOARDED-OUT CHILD

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THE MEDICAL ORGANIZATION OF THE BOSTON CHILDREN'S AID SOCIETY AND THE CHURCH HOME SOCIETY

Any organization which undertakes the foster-care of destitute and needy children assumes great responsibilities. The children come from every sort of home and social condition, and present a great variety of social and medical problems which are very much interrelated and have to be understood and adequately treated if the child is to be helped. The question of determining the health of the children at the time they are received into the care of the societies is a first consideration. This involves, primarily, a record of the previous history of the child and its social surroundings, and if conscientiously done should include data in regard to the parents, other children in the family, and frequently other relatives. The individual child whom we take into our care cannot be regarded as an independent problem. Its welfare is inevitably bound up in that of the parents, brothers and sisters. Exposure to tuberculosis, gonorrhea and other infections, the hygienic surroundings of the child, the financial resources of the family, and similar conditions must all be taken into consideration if an intelligent disposition of the individual child is to be made. This investigation is the responsibility of the reception department of the respective societies, and while not strictly medical in all its aspects, is absolutely indispensable to our medical point of view.

From the time the child is admitted as a ward of the society it is, of course, a social problem, but it is also very largely a medical problem. The preventive clinic is concerned primarily with the medical problems presented by the children. It makes diagnoses, directs the treatment, and indirectly helps to shape up the special services to the social case workers of the societies in their relations to the children. For example, a delinquent boy referred by the courts, found to be

suffering from a heart lesion, must necessarily be protected from certain forms of disciplinary training that would be highly proper and desirable in the case of a healthy boy.

In the carrying out of this medical supervision of the children coming under the care of the two societies mentioned certain necessary steps must be followed:

1. A complete physical examination of the child on entrance.

2. Correction of defects which have interfered with its proper development and nutrition.

3. The prescription of proper diets and feeding, especially in the care of infants and young children.

4. Special supervision of the feeding of infants who are deprived of their mother's milk; or those who are being adapted to second or third year diets.

5. Provision for meeting promptly cases of acute illness in the foster homes; for transferring serious cases and for the early detection and isolation of acute contagious diseases.

6. The examination of the child on discharge from the society, with careful analysis of the history, both for purposes of determining the efficiency of the medical supervision, and possible ways in which it might be improved.

7. Regular consultations with nurses and social workers for the purpose of discussing the general medical aspects of the particular child-caring work that is being done.

8. Conferences with the foster-mothers where they are doing special medical work for particular children, the success of which is dependent upon their intelligent understanding of many of the medical aspects which the case involves.

9. Systematic checking up by the medical director and his assistants of information which seems to question the reliability and fitness of foster-mothers for their important task. Very frequently the only index to the fitness of a home is evident in the child's physical condition, its failure to increase in weight, etc.

10. Statistical study as a whole of all children cared for, in order that the results obtained may be intelligently judged and better methods established.

Our experience in the last three years has demonstrated that many of the children brought to us, while not acutely ill, are in a condition which sooner or later will result in serious trouble. The most common conditions met with are malnutrition, dental caries, hypertrophied tonsils and adenoids, spinal curvature of postural origin, flat feet, skin diseases and defective vision. It is obviously our duty to correct these conditions at the beginning, and to do so it is necessary to have the facilities of a general hospital service in order that the special needs may be adequately met.

The Children's Aid Society and the Church Home Society, caring for an average of 350 and 200 children, respectively, and reaching jointly through their foster home care a total of approximately 800 different children a year, have affiliated with the Boston Dispensary, where every facility for accurate diagnosis and special treatment exists; such as diagnostic, clinical and roentgen-ray laboratories; orthopedic, skin, eye, nose and throat, dental and nerve departments.

The preventive clinic is, therefore, a joint department, supported by the three agencies. The preventive clinic has its own organization, with special physicians, social workers, stenographer, and its own receiving and examining rooms.

The clinic is preventive in the sense that every clinic is, in that it not only diagnosticates and treats acute and chronic conditions, but attempts by a carefully followed up system to apply the principles of prophylaxis wherever possible. It attempts to deal with all the problems which the individual child presents which may interfere with the normal development of health and nutrition.

It has been found by experience that more consistent and systematic supervision and treatment may be obtained when the children that are coming into the care of these two societies are handled from their own special clinic, than when they are passed through a general outpatient clinic or are taken care of in the private office of a physician. The chief reason for this lies in the fact that the same physician and workers are responsible for the children and in the course of time develop a greater degree of interest in the group; whereas in the ordinary routine of an outpatient department they are likely to be looked on as medically uninteresting, which point of view sooner or later works to their disadvantage.

The organization of the clinic may be considered in more detail by separating it into groups, all of which are under one management

but with responsibilities sharply defined. The two children's societies have offices located outside of the dispensary building. Their general offices are concerned with social, financial and administrative details of their work. With them rest the selection of cases, the study and social diagnosis of families; the preparation of histories of children received; the selection of foster homes into which the children are to be sent; the supervision and training of foster parents; the selection and training of the non-medical workers; the social case work supervision of medical workers; the provision and distribution of special food, etc., which is a result of their own observation, or that of the medical director, are found to be necessary.

The preventive clinic at the Boston Dispensary is organized under the control of the medical director of these two societies, whose duties are those of a consultant in all cases involving special decisions or judgments, and who also directs, as his particular charge, the feeding of infants and undernourished children. The routine examinations and home visits are largely made by a full time physician, at present Dr. Leslie H. Macmillan. Her mornings are spent at the Dispensary making first examinations and re-examinations; her afternoons in visiting in their homes children who are reported by the visiting nurses or social workers as ill, but not ill enough to necessitate hospital care.

Both societies follow the plan of having trained graduate registered nurses for the medical social supervision and training of all their children under the age of 3 years. The assistant physician keeps the director particularly informed of the progress of all problem cases and children who are in any way below par. When conditions press more responsibility on the foster mother than her experience justifies, the child is ordered to some hospital. So far as possible the children are transferred to the Children's Hospital Department of the Boston Dispensary, where they come under the immediate care of the director. Contagious cases are sent to the special hospitals; older children are sent to other institutions, or wherever they can be most effectively treated. Upon their discharge from the hospital they are again brought to the preventive clinic and examined in the light of their recent illness, and their disposition and subsequent treatment is determined by the director.

The importance of an all-time physician cannot be overstated; for no consultant of experience could give the necessary time for the daily routine examinations and treatment. A woman physician,

on the whole, fits into the place better than a man, for much of her work is with young girls and young unmarried mothers, whom she is better fitted to influence. The older boys, especially those over puberty, have their first complete examination by the director or by some other man physician at the dispensary designated by him.

Notes on all examinations are made in triplicate. One copy goes to the office of the society responsible for the child, one to the Dispensary general record file, for the benefit of other clinics to which the child may be referred for diagnosis or treatment, and the third is kept on file in the preventive clinic office. The central office is thus informed automatically of everything that transpires in the hospital clinics, and can utilize the knowledge thus obtained in their follow-up social work and in the final disposition of the child.

A child on entrance is subjected to a thorough physical examination and is referred to special departments when the director or assistant physician thinks it is desirable. When this is done a worker in the clinic personally conducts the child to the chief of the special clinic, calls his attention to the particular points under discussion, and gets a decision promptly and without waiting her turn. If the case is urgent, as for example where carious teeth or diseased tonsils must be removed, the director recommends that the child be placed by the society in some foster home accessible to the hospital, so that its attendance may be enforced with the minimum of inconvenience to the child and to the central office; for the latter is under obligation to see that the children are brought to the clinic as often as the director or assistant physician requires.

The assistant physician visits each home within a certain radius of Boston every month or two, and oftener if the condition of the child indicates some special condition calling for her attention. These visits to the foster homes produce many results, not the least important of which is the training and education of the foster parents, especially the mothers, in providing really expert care for very ill and very needy children. This visiting by the assisting physician represents a definite medical survey in many of the foster homes, and results in information of very great importance for the social case workers who are operating from the offices of the respective societies.

The foster mothers report all cases of illness to the general office of the society with which they are associated, and someone at this office communicates immediately with the assistant physician. She

acts on her own initiative, generally visits the child and reports to the director when the illness is serious or involves some special judgment. If the case is too far removed from Boston to be visited, the foster mother calls in a local physician, with whom the central office of the society keeps in touch, and if necessary the director communicates with him also.

There are constantly in the care of the Boston Children's Aid Society anywhere from 60 to 100 infants, and a smaller number in the care of the Church Home Society. These infants are placed in foster homes at board. This group presents particular problems separate from those of the older children, and to meet them there is a special baby clinic under the immediate supervision of the director. This group requires experience and judgment in the matter of substitute feeding, for very few of these babies have mothers to nurse them. It is in such a group that the greatest danger lies, and in which a child-placing agency without medical guidance is bound to go far astray. However experienced a nurse may be, she needs the direction and supervision of an experienced physician. The difficulties of handling such a group are great. The physical exertion and expense involved of transferring so many babies to a feeding clinic from widely separated foster homes would be very costly. We have organized the preventive clinic for these cases with the idea of getting the maximum supervision with the minimum expense and trouble.

The babies are divided into two groups, each visited by an experienced trained nurse. All babies are examined in the clinic at the time they are accepted by either of the societies. The details of feeding are then carefully formulated and the child is placed in its foster home. The nurse visits each home once a week, or once in two weeks, examines and weighs the baby, goes into details of the hygiene and preparation of the feeding with the foster mother, and makes on special record blanks, notes of the case, and on a weight chart plots the weight curve. Once a week the two nurses meet the director in conference. Each case is carefully reviewed and changes made in food, and the nurses instructed in the principles underlying the changes. They are given directions when next to report.

The foster mothers are always in telephone communication with the nurses. Any unfavorable symptom is reported. The nurse visits the child, gives direction herself to the foster mother if the condition is not serious; otherwise reports the case to the assistant physician,

who visits the child. If in her judgment it is necessary, she reports to the director and he either prescribes the treatment or orders the child to be brought to the clinic for his own examination, or arranges for its admission to the hospital. The results of this close supervision are seen in the low mortality rate, and in the almost normal development of the babies, even though bottle fed. The educational value of such a system of supervision upon the foster-mother, the social worker, nurse and doctor, is very valuable and points the way by which large groups of destitute babies may be successfully reared with institutional care with minimum expense and with a comparatively simple organization.

There is in this statement no implication that our method of tackling a difficult problem is peculiar to Boston, or is not in force in similar or better degrees in other cities. It is made in the hope that by comparison of notes of methods employed and results obtained, free discussion will lead to more efficient care of the children in our own and other child-placing agencies.

STATISTICAL STUDY OF THREE YEARS OF SUPERVISION, 1916 TO 1919

The results of the statistical study of three years of medical supervision are given in the appended summaries. They show an average of about 500 children a year cared for. Of these, 15 per cent. were sufficiently ill from one cause or another to be admitted into the Children's Hospital wards, which may be taken as a fair estimate of the hospital requirements of such a group of children. A little less than one third of these admittances were for necessary adenectomies or tonsillectomies. The low death rate of the group undoubtedly was influenced by the prompt detection of serious cases of illness and the facilities provided for early, and when necessary, prolonged hospital care.

The mortality statistics are interesting in the proof they offer of the practicability of reducing the death rate in a supervised group of children to a point below that which is accepted as normal for the community. A total of only seventeen deaths in three years among 1,531 cases cared for in that period amounts to about one death per year for each hundred children under our care. It would be interesting to compare this mortality rate with that of child placing agencies who have not developed systematic and thorough medical

supervision. We have included all deaths in children who have been accepted by the society, whether hospital cases or not; and as the medical department does not attempt to say whether a child shall or shall not be accepted, there has been no temptation on our part to exclude poor medical risks.

Equally interesting are the figures showing the effect of the special feeding clinic in the nutritional development of the children in the first and second years. We have included only babies who remained in our care for at least one month. All the babies were fed on modifications of cow's milk, prepared in the foster homes and supervised by visiting nurses under medical direction. Seven tenths of them gained in weight considerably above the normal rate of the average healthy infant, and three-tenths only failed to equal the normal rate by a small margin. The conclusion one is justified in drawing from this experience is that with proper organization and intelligent direction, the boarded-out baby, even though deprived of its mother's milk, is a perfectly good medical risk, and need not be deprived of its fair chance in life. There were only seven deaths in three years in 171 babies followed for an average of 13.6 months, and three of these only were from disease connected with digestion and nutrition. Fully as many cases, not included in the series, were carried for less than one month without any mortality.

CASE HISTORIES

The following brief case histories are fair examples of a few of the problems involved in the medical supervision of a group of children such as we are caring for in the preventive clinic.

CASE 1.—M. K. was transferred to the B. C. A. S. from the Children's Hospital at the age of 13 weeks, 3½ pounds under weight, as a typical feeding case, presenting no particular difficulties of digestion. She remained in the care of the society until she was 13 months old, at which time she weighed 23 pounds, or one pound above the normal weight. During this time she contracted bronchopneumonia, making an excellent convalescence. The weight chart shows the characteristic gain of a typical undernourished infant, who was perfectly capable of responding to careful, rational substitute feeding.

CASE 2.—C. W. was admitted to the Church Home Society at the age of 7 years in March, 1919. He came from a home where the environment was of the worst. His mother was a sexual degenerate and the child acquired much undesirable sex knowledge, practiced masturbation and was morally deficient. He lied, stole and was filthy in his habits. Physically he was 12 pounds below weight, had enuresis, defective vision, phimosis and functional disturbance of the heart.

The boy was placed in an excellent home and his physical defects attended to. He had been cured of enuresis and masturbation, his habits improved and he has gained 11 pounds in less than one year, that is to within 6 pounds of his normal weight development. The boy's whole attitude toward life has been changed. The case illustrates well the equal importance of social and medical care. This child was well started on the road towards complete moral degeneracy and physical debility. There appears to be no fundamental mental defect; the fault lying in the social environment with consequent physical deterioration.

CASE 3.—F. K., female, aged 9 years 10 months, full term normal delivery; breast fed for 13 months. Has had pneumonia three times with a nephritis in 1914 which followed an attack of pneumonia. Measles at 20 months, whooping cough at 5 years, tonsils removed at the age of 4 years, and first attack of chorea at the age of 5. Was a patient at the Children's Hospital Outpatient Department with chorea from April, 1913, until December, 1914, at which time she was discharged in good condition. August 8, 1918, she reappeared in the Outpatient Department with a history of two attacks of pneumonia since 1914. Chorea reoccurred in July, 1918. Heart and lungs were negative and she was admitted to the wards August 8. The physical examination on admittance showed her to be a well developed and nourished child with marked choreiform movements of the limbs, head and face.

October, 1918, she was discharged from the Children's Hospital and referred to the preventive clinic for medical supervision and for placement in a good boarding home. On admission to the clinic the diagnosis of chorea and a systolic heart murmur were made. The child was placed out in an excellent home and showed a steady gain in weight and general physical condition.

December, 1918, the child had gained 13 pounds and showed no choreiform movements. At this time her parents wished her to be at home so was discharged from our care and referred back to the Outpatient Department of the Children's Hospital for observation. During the spring of the year there was a return of the chorea. For this reason she was again referred to the B. C. A. S. and the preventive clinic for care and placing out. At the time of the second admission in July, 1918, there were definite choreiform movements. At this time only a slight impurity of the heart sounds was noted. She was again placed at board. December, 1919, the heart condition had entirely cleared up but a few incoordinate movements were still noted. February, 1920, shows the child to be in very satisfactory condition, showing no heart abnormality or choreiform movements. This child gained 21 pounds in seventeen months. Her present condition indicates a complete recovery from chorea with no cardiac complications. This is the type of case which, under unfavorable conditions, develops repeated attacks of chorea with serious endocarditis and either permanently impaired health or fatal complications.

CASE 4.—E. N., female, aged 10 years; born Aug. 23, 1908. Mother died of pulmonary tuberculosis. Past history negative; had none of the children's diseases. Because of necessity of the mother being in a sanatorium, the father was unable to keep the home together so placed the children out.

Aug. 29, 1918, the child was admitted to the preventive clinic. Admission examination showed a slender, somewhat undernourished girl of 10 years. Underweight and underheight. The tonsils were moderately enlarged. The lungs showed signs of an arrested tubercular process in both apices which was confirmed by a roentgenogram of the chest and a positive von Pirquet reaction. The child was placed in a favorable environment and special empha-

sis put on nourishing food, fresh air and good hygiene. She made excellent progress until February, 1919, when she had an attack of acute tonsillitis followed by acute arthritis and endocarditis. She was in bed for several weeks but entirely recovered although a very decided heart murmur persisted. The tonsils and adenoids were removed in June, 1919, from which the child made an excellent recovery.

She now shows no signs of any lung condition, is over weight, and the heart murmur is scarcely audible.

This type of case shows the excellent result possible to obtain in a child with definite quiescent tubercular infection. At the period of adolescence it would have been quite possible for the tubercular process to have become active had not the child had proper medical and social supervision. Despite this tubercular handicap, the child came through an attack of rheumatic fever with no serious heart complication. Ten months later she was 7½ pounds above the normal weight and perfectly well.

Had this child continued in an unfavorable environment, the outcome would, in all probability, have been quite different. Taken in the early stages, before the child's vitality is too greatly impaired, put into a desirable home with intelligent supervision, these children respond favorably to their environment, and often surpass the normal standards of health.

CASE 5.—J. F., male, aged 15 years, was admitted to the preventive clinic July 6, 1917. Had measles as a child and rheumatism in 1914. Following this there was an attack of endocarditis which has left a permanent mitral regurgitation. At the time of admission there was found a mitral regurgitation. This increased in severity, partly due to the boy not following directions given him concerning the amount of exercise allowed.

December, 1918, a diagnosis of double mitral lesions was made and strict directions as to the type of work and recreation to be allowed. Since that time there has been a gradual improvement. June, 1919, the heart murmur was not marked. His improvement has been very gratifying.

His gain in weight has been good. Weight on admission was 104½ pounds and at last visit was 143½ pounds, showing a gain of 39 pounds in two and a half years. This type of case of a chronic heart lesion shows the necessity for constant observation and control of muscular exertion and condition. At no time was there a break in compensation which so often occurs in heart conditions of this severity. By intelligent care and supervision both as to the boy's general physical condition and his working environment, he will probably be able to lead a healthy and useful life without being a burden to himself and the community.

A TWENTY-FOUR HOUR SCHEDULE FOR SCHOOL BOYS *

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In a previous communication [1] I drew attention to certain fundamental principles with reference to the care of the health of school children, and pointed out lines for further extension of health supervision. It was stated that "there must be a general recognition of the importance of health and a realization among the school authorities that the health of children is as important as scholarship," and that there was "special need in securing the cooperation of parents in protecting the health of their children." I also presented a table of the distribution of the boy's time during school hours between study, activity and inactivity. I am convinced by a further use of the table that it gives a correct distribution of the boy's school time. It became obvious, however, in the application of this table to the individual child, that no satisfactory plan for the boy could be made without a coordination of the school schedule with the time that the boy spent away from school.

The child may be considered as the center of a triangle, the base of which is represented by the home and the two sides by health and education. The parent, the physician and the teacher are together responsible for the child's life, and no part of that life can be arranged intelligently without the cooperation of all three individuals. For instance, the child's physical environment, such as buildings and fresh air, is dependent not alone on the proper sanitation of the school building, but on the room in which he sleeps at home. His nutrition is maintained not only by the school lunch and the dinner received at school, but also by the breakfast and the supper given at home. His educational work in school must be arranged, bearing in mind not only the studies necessary for the school curriculum, but also whether or not he is doing work at home, such as studying music and languages. His exercise is made up of what he does at home in the afternoon

1. A Health Study of a Boys' School, Am. J. Dis. Child. **18**:246 (Oct.) 1919.

quite as much as of the carefully arranged athletics at school. His periods of relaxation at school and at home together make up the relatively inactive portion of his day.

During the last year, at Mr. Rivers' Open-Air School for Boys, we made a study of the weekly twenty-four hour distribution of the time of the boys. This study was made possible only because of the active interest in the boys' health taken by the principal of the school and the hearty cooperation of the parents. The matter of time distribution and the question of nutrition are the two most important factors in the health of school children.

There are many guides to the study of nutrition and there are tables of standards of normal development. There is no means at present of determining whether a given child is distributing his time in conformity with a healthful arrangement. It seemed to us that it was worth while to attempt to prepare a table of what appeared to be a reasonable and healthful division of the hours of the week. It was thought that such a table might serve in much the same way as the tables of normal weight and height are used to measure nutrition. The weight and height tables do not furnish the sole method of estimating a child's nutrition, but they do give an average standard with which the individual child may be compared.

Tables 1, 2, 3 and 4 were prepared after a study and comparison of the time distribution of the children of various school ages. The data for the tables was secured from the actual school schedules and the statements of the parents concerning the time spent at home. After the tables had been made, as many of the boys as possible were checked against them as a control. We believe that they represent very nearly the proper distribution of time for boys of the ages indicated. The figures may need to be modified later, but those entered here represent the facts as nearly as could be determined with the present information. They are submitted in the hope that they will be of use in planning the daily program of school boys. If they are tried out by many different people their value and accuracy can be determined.

In attempting to make a weekly plan for school boys, the first division of time comes between that spent at school and that spent at home. The home time is partly on school days and partly at week ends. Five days out of the seven the boys are in school, and during these days the parent and the teacher share in planning his routine.

TABLE 1.—Weekly Schedule in Hours for Schoolboys, Aged 6 Years

		School Days		Week Ends	Weekly Total	
		School	Home			
Activity	Study	14	0	0	14	40½
	Exercise	7	7½	12	26½	
Inactivity	Relaxation	10½	21	12	43½	127½
	Sleep	0	60	24	84	
Total.		31½	88½	48	168	168

TABLE 2.—Weekly Schedule in Hours for Schoolboys, Aged 8 Years

		School Days		Week Ends	Weekly Total	
		School	Home			
Activity	Study	17	0	0	17	48½
	Exercise	8½	9	14	31½	
Inactivity	Relaxation	9½	18½	11	39	119½
	Sleep	0	57½	23	80½	
Total.....		35	85	48	168	168

TABLE 3.—Weekly Schedule in Hours for Schoolboys, Aged 10 Years

		School Days		Week Ends	Weekly Total	
		School	Home			
Activity	Study	21	0	0	21	55
	Exercise	10	9	15	34	
Inactivity	Relaxation	9	16	11	36	113
	Sleep	0	55	22	77	
Total.....		40	80	48	168	168

TABLE 4.—Weekly Schedule in Hours for Schoolboys, Aged 12 Years

		School Days		Week Ends	Weekly Total	
		School	Home			
Activity	Study	22½	0	0	22½	62½
	Exercise	12	12	16	40	
Inactivity	Relaxation	5½	15½	11	32	105½
	Sleep	0	52½	21	73½	
Total.....		40	80	48	168	168

For two days at the week-end they are at home all the time and the parent alone is responsible. The particular school in which these studies were made is a country day school, so that the hours at school are long. None of the boys under 14 years of age are given home work. If a boy goes to a one session school, the figures for school days will need some adjustment to meet that situation, but the adjustment should be made taking into account all the factors and remembering also that there are seven days in the week.

The boy's time may be considered from another point of view as divided between activity and relative inactivity. His activity takes the form of study and exercise. His inactivity consists of sleep and relaxation. Relaxation is not a very satisfactory term, but we have been unable to find a better one to describe the time that is spent in dressing, in eating, in reading, etc. These periods require comparatively little expenditure of energy.

In the distribution of the boy's active time there is room for considerable variation, but the school curriculum makes it necessary for him to cover a certain amount of work, therefore, there is an irreducible minimum in the hours of study. Since he must have some exercise every day, there is an irreducible minimum in this factor also. How wide the variations in these two particulars may be is a matter not definitely determined. The figures which we have put down represent what the average healthy boy of a given age can do who is taking enough school work to advance in his grade and who is having sufficient exercise to keep in good condition.

In his inactive period the factor of sleep should not be below what is entered on the table. Sleep is the time during which there is a restoration of energy in the body. It acts much like the charging of the batteries which keep the electric mechanism of the automobile working satisfactorily. We cannot afford to draw too heavily on the reserves of the body. If we do, continuing the simile, our batteries will become discharged and the engine will not run.

The inactive periods should represent a balance against the periods of activity. The distribution of time between the two groups, activity and inactivity, should bear a fairly constant relation. A boy who is having a disproportionate amount of activity as compared with inactivity may be able, because of his unusual endurance, to carry through the schedule. He may be maintaining his undue activity, however, at the expense of his reserve, and eventually his health will suffer as a

consequence. He may have a proportionately large amount of activity during the five school days, and yet because of an inactive week-end establish a normal weekly balance. Individual variations from the standard will undoubtedly occur, but when such variations are present, there should be some compensating consideration which would make the divergence from the average reasonable. It is possible for a child to have a weekly schedule different in every respect from the average and yet be in normal health and progress satisfactorily in school. Such a child is obviously unusual and certainly could not be taken as a model for others to follow.

We believe that the principles involved in these tables are correct. We hope that they will be used sufficiently so that correct figures may be inserted, if those given here prove to need modification. The study represents a cooperative effect on the part of teacher, parent and physician to plan the entire program of the child as a unit giving equal consideration to education and to health.

DISCUSSION

DR. FLEISCHNER: Dr. Holt expressed himself very earnestly about this work last year. Work of this sort is a definite contribution to pediatric knowledge. We have taken too many things for granted and have let boys run along on schedules about which nobody knew anything. Figures like these are a definite step forward not only in preventive pediatrics, but in connection with educational results. I am sorry Dr. Dodson could not have remained for he might then have seen that there are a few of the members of the society very much interested in the question of cooperation between educational and health workers.

DR. BLACKADER: I have listened with pleasure and profit to this paper. For many years I have felt that as physicians and physiologists we have not exerted sufficient influence in the councils of our school boards. In Montreal, I have protested frequently against the length of the school hours. Parents are desirous that their children should have a broad education, a much broader one than they themselves had; and one subject after another is added to the curriculum. Still further, when the regular school hours are over, music, dancing, and sometimes a French master, occupy more of the precious daylight hours in the winter months. I am afraid that some of the unfortunate failures in life of which we heard this morning may in part be due to this attempt to prolong mental training at the expense of physical training.

I desire to convey my thanks to Dr. Smith for having added in this paper to our knowledge of how the education of a child should be conducted. The cramming of a multitude of facts into the brain of a child to enable it to pass an examination to the honor of the teacher is not desirable; the results are often disastrous when the school hours occupy almost the whole of the daylight. In the long winter, school begins at 9 a. m., and with the exception of an hour and a half at midday, lasts till 3:30 p. m., and if the lad's lessons have not been learned, or some breach of discipline has taken place, he is obliged to remain in for another hour, and the last hour for play and open air exercise vanishes.

It is high time the pediatric society makes its opinion heard, and its influence felt, not only in the United States but in Canada.

DR. HEIMAN: I would like to know whether the time spent in getting meals is placed in the exercise and relaxation period. I ask this because if there is one pernicious practice it is the shortness of the lunch hour in the public schools. I think we should endeavor to remedy this evil.

DR. EATON: I believe Dr. Smith's work has opened a new field to which he has not referred in describing his schedule. He has enabled the child to do the best possible work in the best possible environment and to therefore get the fundamentals thoroughly learned first. It has been my experience that under our modern methods we are not paying enough attention to physical development or to the relation between physical and mental development. We have pushed so far in one direction that we have neglected the other, and the fundamentals have therefore not been well learned. It is impossible to erect a good edifice on a poor foundation. Dr. Smith has laid the foundation upon which to erect an edifice of mental and physical health, a plan which if carried out will help the child through his educational endeavors with the best results.

DR. SMITH: Answering these questions about method, it seems that the only way to get anywhere is to get the cooperation of the school principal. Under the plan outlined the principal never makes any changes or modifications, not even a change in the lunch hour, without consulting the medical authorities. We must make it understood that health and education go on hand in hand. The meals come in the period set apart as relaxation. Relaxation means everything which is inactive as compared with exercise and study. I shall be glad to see if these figures are correct and if they are not correct I should like to modify them. My only thought was to have a standard for comparison with the individual child and to see if he conforms to what is believed to be a correct distribution of time.

THE FATE OF SUBCUTANEOUSLY INJECTED RED BLOOD CELLS*

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PART I.

Modern methods of intravenous transfusion are so satisfactory that today the question of using an extravascular route arises in infants only. A study of the older writings shows that at different times and places both the subcutaneous and intraperitoneal routes were employed and in the opinions of the reporters usually with success. My interest in the subject arose from observations made on two patients who were injected subcutaneously after unsuccessful attempts at intravenous transfusion. One of the patients, whose cells were never greatly diminished, showed a decided rise in hemoglobin, and the second patient showed a marked rise in both hemoglobin and cells. Unfortunately for the experiment, however, both patients were given iron. I then purposely employed the subcutaneous rather than the intravenous route in three patients who received no drug. The blood was citrated. With the exception of Ann F., who was given blood from her mother, all patients' blood groups were determined and a blood given whose corpuscles would not be agglutinated by the recipient's serum.

Two were University Hospital patients and on them was made the study which is reported in the second portion of this paper. The pertinent clinical data from all five cases is presented in Table 1. The Dare hemoglobinometer was used in the three private cases and the Fleischel-Miescher instrument was used in the University Hospital cases. The hemoglobin and red blood cell estimations were made in the private cases by a trained laboratory technician, and in the University Hospital cases by Dr. Ott, the resident in pediatrics. The results are as reliable as one can expect from the method employed.

It is apparent that the injection was usually followed by an increased hemoglobin percentage.

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PART II.

Karst,[1] in 1873, noted that blood injected subcutaneously caused a transitory swelling only—and hastily concluded that it was absorbed into the circulation. Later workers, Bareggi,[2] Orth,[3] Müller[4] and others, showed that after such injections, the more remote as well as the neighboring lymph glands became swollen and engorged with blood cells, and that within an hour thereafter large numbers of red blood cells were to be found in the thoracic duct.

As bearing on this point of the absorption into the circulation of extravascularly introduced blood, it is to be noted that Hayem[6] after peritoneal injection of dogs' blood into goats recovered dogs' corpuscles from the circulating blood of the latter.

Recently Scott[6] and Hanson injected stained foreign corpuscles subcutaneously and later found them in the recipient's circulation. We can accept as proven the thesis that subcutaneously injected red blood cells are qualitatively capable of reaching the recipient's circulation.

How many cells do so?

It occurred to me that the method devised by Ashby[7] for determining the length of life of the transfused corpuscle offered a way to the solution of the problem.

The method was applied in the two University Hospital cases, Nos. 16706 and 16895. The bloods of these two patients were in Groups III and II. Before receiving the blood injection, their own blood cells were counted, Group II serum being used as a diluent in the hemocytometer in the first case, and Group III serum in the second. Counts of the unagglutinated cells were made on the day preceding the injection and on the first and fifth days thereafter.

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1. Karst: Injectionen von defibriniertem Blute ins Unterhautbindegewebe, Berl. klin. Wchnschr. **10**:587, 1873.
2. Bareggi: Arch. per le scienze med. **7**, No. 4, quoted by Wm. Hunter, op. cit.
3. Orth: Beitrag Zur Kenntniss des Verhaltens der Lympdrüesen bei der Resorption von Blut-extravasaten, Virch. Arch. **56**:269, 1872.
4. Müeller: Untersuchungen üeber das Verhalten der Lymphdrüesen bei der Resorption von Blut-extravasaten, quoted by Wm. Hunter, op. cit. 1879.
5. Hayem: De la transfusion peritoneale. Compt. rend. **88**:749, 1884.
6. Prof. F H. Scott, personal communication.
7. Ashby: The Determination of the length of life of transfused blood corpuscles in man, J. Exper. Med. **29**:267, 1919.

TABLE 1.—Clinical Data

Case	Diagnosis	Age	Amount Blood Injected, C.c.	Body Weights and Red Blood Cell and Hemoglobin Estimations													
				Before Injection			1 Week After Injection			2 Weeks After Injection			3 Weeks After Injection			4 Weeks After Injection		
				Weight, Gm.	Red Blood Cells	Hemoglobin, per Cent.	Weight, Gm.	Red Blood Cells	Hemoglobin, per Cent.	Weight, Gm.	Red Blood Cells	Hemoglobin, per Cent.	Weight, Gm.	Red Blood Cells	Hemoglobin, per Cent.	Weight, Gm.	Red Blood Cells	Hemoglobin, per Cent.
Marj. G. Received iron	Rickets, anemia	10 mos.	75	6,750	4,712,000	27	.....	.....	....	6,750	.....	47	.....	.....	....	6,825	.....	66
Paul H. Received iron	Celiac disease	2½ yrs.	100	7,960	2,776,000	43	9,000	3,900,000	50	.....	.....	....	9,000	3,984,000	6 8			
Ann F.	Anemia	8 mos.	60	6,250	4,630,000	25	.....	.....	....	.....	.....	....	.....	.....	....	6,775	4,200,000	35
Univ. Hosp. No. 16706	Purpura hemorrhagica	7 yrs.	130	26,000	4,750,000	75	.....	.....	69	.....	4,270,000	73						
Univ. Hosp. No. 16895	Hemophilia	2 yrs.	100	13,400	5,200,000	47	.....	.....	60	.....	4,420,000	70						

Ashby's technic was followed exactly—and all counts were made in duplicate and accompanied by control counts to check the continued agglutinative capacity of the serum.

Table 2 presents the results. In the last column is shown the estimated number of unagglutinatted cells per cubic millimeter which would have been present had all the injected blood cells reached the recipient's circulation. It is evident that this number was never approached and that even five days after the injection the number of unagglutinatted cells was not definitely increased.

TABLE 2.—COUNTS OF UNAGGLUTINATED RED BLOOD CELLS BEFORE AND AFTER INJECTIONS OF GROUP IV BLOOD, THE COUNTING MEDIA BEING AGGLUTINATIVE TO THE RECIPIENT'S OWN CELLS BUT NOT TO THOSE GIVEN HIM

Case Number	Weight, Kg.	Recipient's Own Blood Group	Serum Used as Counting Medium	Amount Blood Injected, C.c.	Numbers of Unagglutinated Corpuscles per C.c.			
					Day Preceding Injection	Day After Injection	Five Days After Injection	Theoretical Number if All Injected Blood Had Been Absorbed
16706	27.0	III	II	130	48,400	50,550	100,350	350,000
16895	13.4	II	III	100	189,750	132,825	162,450	780,000

Recently, after consultation with me, Giffin and Ashby, at the Mayo Clinic, carried out a similar experiment on an adult who had pernicious anemia. Dr. Ashby has sent me the results with permission to publish them. The patient received 250 c.c. of blood subcutaneously. His average initial nonagglutination count was 50,000 and the post-injection count was 97,350. Ashby estimates that the increased number of cells should in this case equal 250,000 and states that if any of the blood got into the circulation it was only a fraction.

This is entirely different from Ashby's results on intravenously transfused individuals as reported in her work on the length of life of the transfused corpuscle. For example, the initial nonagglutination count in one patient, an infant weighing 20.5 pounds, was 54,400. He was given 220 c.c. of blood, and his unagglutinated cells rose to 1,175,000.

Subcutaneous injection of blood is usually followed by a rise in hemoglobin percentage: but only a small fraction of the cells so injected reach the circulation of the recipient.[8]

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8. The following references may also be consulted:
Hirsch: Ueber subcutane Blut-transfusion nach der von Ziemessenschen Methode, Berl. klin. Wchnschr. **25**:790, 1888.
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Sicard: Homohémothérapie sous-cutanée, LaPresse méd., **33**:304, 1918.
Hunter, Wm.: Intraperitoneal Blood transfusion and the Fate of absorbed blood, J. Anat. & Physiol. **21**:138, 264, 450, 1886.

A PRELIMINARY REPORT OF THE STUDY OF BREAST FEEDING IN MINNEAPOLIS*

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Most of the members of this organization have heard me in season and out of season, talking about breast feeding, and the study we have been making of it at the University of Minnesota. Although the statistics will not be ready until September, enough data have come so that we have records which indicate what we have learned and accomplished. I have had so many inquiries in regard to our technic, that I am taking this opportunity to explain the essential parts to those who are interested.

The investigation of breast feeding in Minneapolis was planned to study the wider applicability of certain principles of breast feeding which we have been using at the University of Minnesota and in private work. We wished to see whether these principles are applicable to a wider field, and to all strata of society. We wished to make a statistical study to observe the effect, if any, on infant mortality. Dr. Rood Taylor made a study of the records of our New-born Clinic at the University recently and he found that in one thousand consecutive cases in which the mother and the baby left the hospital together each child was at the breast. This disposes of the importance of the bogey, agalactia. The idea that the mothers often have no milk for their new-born babies was not given much consideration in this study. The technic of the maintenance and reestablishment of breast feeding is that which I described in my chairman's address in New York in 1917[1] and I shall mention simply the essentials here.

The demand which is made on the breast is by far the most important factor in the maintenance of the breast milk supply. Repeated, regular and complete evacuation of the breasts by a vigorous baby, is, of course, the natural and best method. When this natural stimulus

1. Establishment, Maintenance and Reinstitution of Breast Feeding, J. A. M. A. **64**:417 (Aug. 11) 1917.

is not obtained or when the demand on the breast is insufficient for any reason, the supply of breast milk dwindles gradually until the breast does not support the baby. In these cases artificial aid is necessary. In an interesting paper published in 1913, Zlocisti showed that this can be accomplished by putting the father at the breast, and stimulating the lactation systematically. This has, however, many esthetic and social objections. We have found that in most cases, using the principle of stimulation but by milking the breast, we are able to accomplish a similar or even better result. A cross section of the breast shows that the milk sinuses are largely just back of or in the area under the colored areola. The gland proper is farther back. We apply the same principles that the milk maid applies. She does not stroke the cow's udder. She grasps the teats only. We do not massage or stroke the breasts over the glandular tissue as this often causes injury. We grasp the breast just back of the colored areola, press the forefinger and thumb together, thus closing off the sinuses. Using a milking motion, push forward then outward, thus emptying the ducts and sinuses to the nipple itself. This should be done gently and should not be painful. Very little trauma should be done the nipple and the gland tissue of the breast itself is not injured.

Let us consider the premature baby first. Many a premature baby has been deprived of its mother's breast milk unnecessarily. The milk of the mother of the premature baby dries up, not because of the baby being born prematurely, but because the premature baby cannot make the proper demand on the breast. We make the practice of milking the mothers breasts as described above, and giving the milk to the premature baby, usually by means of a tube. In our experience these mothers of premature babies furnish milk just as well as mothers of full time babies, and in case after case we have found that these mothers who are milking their breasts, and not laying the baby on the breast on account of the weakness of the baby, have just as good a milk supply, and often are able to furnish milk for their own babies and for another baby besides. When we have intelligent mothers who cooperate well we do not at all feel that the breast feeding of the premature baby is difficult.

It may take a little more time but the mothers are almost always sympathetic and willing to aid in this work and do not complain of the extra time involved. Most of our premature babies are fed with a tube for a month or two before they are laid at the breast at all. It is certainly much less trouble than wet nursing.

It is not only in cases of prematurity that this method is of value for keeping the breast milk up. When a baby is weak from any cause, or ill, so as not to be with the mother, or even when the mother is required to be away for a period, as in one case for two weeks, this method will keep the supply up.

When the trouble is with the breast or the nipple itself, this method may be used to advantage. In one case a mother had failed to nurse two children because of a badly inverted nipple on one side. With the third baby she was shown how to express the milk and encouraged in carrying out this procedure over a long period. At the end of nine months, she was nursing the baby at one breast fully and on the other she had expressed the milk at every feeding; five times in every twenty-four hours during the whole nine months period. When she appeared for the weaning of the baby, at the end of nine months she was getting more milk from the breast on which she could not lay the baby, and from which she had expressed the milk regularly, thus furnishing the stimulation artificially, than she was getting from the breast on which the baby was being laid. In cases in which the nipple is sore or where there is a fissure, this method can be used to let the nipple have the proper rest, and at the same time the breast milk is not lost for want of stimulation. Expression can be used without any injury to the nipple itself. It would be a mistake to leave the impression that we depend wholly on expression in this study of breast feeding. Every other method of encouraging and instructing the mothers in breast feeding is applied also. Expression is reserved largely for the more difficult cases. However, I wish to stress the demand made on the breast and the expression as the important means, rather than the very common giving of enormous quantities of fluid. We know enough now about the physiology of the breast, if we could apply it, to get 90 or 95 per cent. of the babies nursed at the breast.

In organizing the bureau for carrying on this study, we began with the medical men. We wrote to every physician in the city announcing the formation of the bureau, we invited them to meet at the University, and explained the purpose; we sent representatives to talk with them and explain all details. We made it quite plain that no physician in active practice would be employed in connection with the work. I was fortunate in that I was confining my private

work to consultation and referred work. Each physician was asked for criticisms. A card index of the physicians was maintained on which any special desire of the physicians was recorded. In most cases the physicians wished that we go directly into the cases, but report to them afterward. Some wished, however, to have us report to them before going in. Some wished all our statements and directions to come through them personally. We respected all these wishes. After we had been in operation some time, we sent a representative to all the physicians again to ask whether we were embarrassing them in any way, and asked for suggestions to prevent such embarrassment. The Minneapolis Health Department cooperated in every way possible; not only passively but actively. The Infant Welfare Society took up the work of getting information for us from the families with whom they were working. Prominent citizens and the daily papers participated and aided in many ways.

The Breast Feeding Investigation Bureau of the Department of Pediatrics of the University of Minnesota was the name under which the work was carried on. The graduate school of the University appropriated $1,000 for the study. The war chest appropriated $3,000. From private individuals and other sources, about $1,500 more was paid, thus making the total amount between five and six thousand dollars for the year's study.

The mother of practically every baby born in Minneapolis during the year was followed for nine months. The birth reports were sent in from the health department every day, and the first information concerning the breast feeding was obtained by telephone or personal call. If things were going well literature was sent each month. If the return cards were not sent back, the case was followed up by telephone or personal call. If there was any trouble with the breast feeding, the bureau was thus informed and the doctor was consulted, a nurse sent out to instruct the mother when necessary, even daily. The literature was as follows:

1. Is your baby being breast fed?.....
2. If not, when and why did you stop?.....
3. How many other children have you had?.....
4. Give years of births: 1..... 2..... 3..... 4.....
5. How many are living?.....
6. If you have lost any, at what ages and from what cause?.....
.....

7. How long was each child at the breast only? (If but a few days or short time, state as nearly as possible the number of days.)
   1..... 2..... 3..... 4.....
8. When was the breast stopped in each case?
   (1).....mos. (2).....mos. (3).....mos. (4).....mos.
9. Give reason for stopping breast feeding in each case if before the ninth month.
   1..... 2..... 3..... 4.....
10. If bottle was given with the breast, when was it begun and was it in addition to each breast feeding or in place of certain breast feedings.
    1..... 2..... 3..... 4.....

I can be reached by Phone No.....

POST CARD

DEAR MADAM:

Summer will soon be here. It is especially important now for your baby to be kept upon the breast. There is much more danger for the bottle-fed baby when the weather is hot.

We wish to make sure again that you have no difficulty with the breast feeding which can be prevented.

We are, therefore, taking the liberty of sending you another card, asking you to answer the following questions and return it to us.

Thank you.

For THE BREAST FEEDING INVESTIGATION BUREAU.

.....

(1) Is your baby still breast-fed?.....
(2) How often do you feed it?.....
(3) Does it receive the breast only?.....
(4) Are you having any difficulty nursing the baby?.....
.....
(5) If so, what?.....
(6) If not breast-fed, when and why did you stop? (State how long the baby was breast-fed.) .....
.....

POST CARD

(1) Is your baby still breast-fed?.....
(2) How often do you feed it?.....
(3) Does it receive the breast only?.....
(4) Are you having any difficulty nursing the baby?.....
.....
(5) If so, what?.....
(6) If not breast-fed, when and why did you stop? (State how long the baby was breast-fed.) .....
.....
.....
.....
Have you or the baby had Influenza?.....
Have you a telephone?.....

A report was got from each child every month.

Such work is usually done in clinics and hospitals, but we reached everybody, rich and poor. We were told, and we also feared, that we would have great difficulty in the private families where the physicians were in charge. This, however, we found not to be true. In almost every case the physician was sympathetic and aided us. When our agents found that there was difficulty with breast feeding we often asked the physician to give us his support, which he almost always did. Many of our workers have reported that they had even less trouble with those who were educated and had means to pay for services of their own physicians and nurses.

Jan. 1, 1920, this work was turned over to the Infant Welfare Society of Minneapolis, thus making it permanent. The final report cannot be given out until nine months after January 1, as babies born in December, 1919, will not be nine months old until September, 1920. The Infant Welfare Society is giving us reports to complete our records.

I would, however, call your attention to the beginning of the report where the total results of the investigation for January, February, March, April and May are listed. The results by months run from 96 per cent. at the end of the second month to 72 per cent. at the end of the ninth month.

TABLE 1.—TOTAL RESULT OF INVESTIGATION OF BREAST FEEDING OF THE JANUARY, FEBRUARY, MARCH, APRIL AND MAY BABIES BORN IN MINNEAPOLIS DURING 1919

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 2,022 babies still under observation at the end of the ninth month	1,472	72+	27+
Of the 2,113 babies still under observation at the end of the eighth month	1,631	77+	22+
Of the 2,240 babies still under observation at the end of the seventh month	1,810	80+	19+
Of the 2,355 babies still under observation at the end of the sixth month	1,992	84+	15+
Of the 2,412 babies still under observation at the end of the fifth month	2,090	86+	13+
Of the 2,505 babies still under observation at the end of the fourth month	2,250	89+	10+
Of the 2,674 babies still under observation at the end of the third month	2,492	93+	6+
Of the 2,847 babies still under observation at the end of the second month	2,761	96+	3+

TABLE 2.—JANUARY, 1919, CASES

Six hundred and thirty-six babies were born in Minneapolis during January, 1919. Of these, at the end of each month listed, the data are shown.

	Jan. 31, 1919	Feb. 28, 1919	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30. 1919
Breast fed	516	486	427	590	345	301	224	146	88
Breast fed complemental*	33	41	67	66	75	94	138	198	242
Total breast fed†	549	527	494	656	420	395	362	344	330
Artificially fed	...	8	24	39	56	80	70	75	85
Total under observation‡	549	535	518	495	476	455	432	419	415
Artificially fed from birth	13	13	13	13	13	13	13	13	13
Baby died	18	21	25	27	28	29	29	31	31
Mother died	3	3	3	3	3	3	3	3	3
Refused to give information	0	3	3	5	5	6	7	7	7
Moved out of town	2	6	13	23	31	40	46	48	49
Cannot be traced	11	15	21	30	40	50	66	75	78
Out of town cases	40	40	40	40	40	40	40	40	40
	636	636	636	636	636	636	636	636	636

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 415 January babies still under observation Sept. 30, 1919	330	79+	20+
Of the 419 January babies still under observation Aug. 31, 1919	344	82+	17+
Of the 432 January babies still under observation July 31, 1919	362	83+	16+
Of the 455 January babies still under observation June 30, 1919	395	86+	13+
Of the 476 January babies still under observation May 31, 1919	420	88+	10+
Of the 495 January babies still under observation April 30, 1919	456	92+	7+
Of the 518 January babies still under observation March 31, 1919	494	95+	4+
Of the 535 January babies still under observation Feb. 28, 1919	527	98+	1+

* By "complemental" is meant breast fed with an addition of some artificial mixture after the breast feeding.

† Sixty-seven mothers of January babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

‡ Jan. 31, 1919, we had 549 of the babies born in January under observation. Sept. 30, 1919, we had 415 of these babies still under observation, 134 of the 549 babies under observation on Jan. 31, 1919, having been dropped for the following reasons: baby died, 13 cases; refused to give information, 7 cases; moved out of town, 47 cases; cannot be traced, 67 cases.

The cold figures are lifeless but, of course, necessary. I have often thought of it in comparison with our judgment of certain therapeutic procedures. The statistics of the effect of diphtheria antitoxin are of interest and, of course, are also necessary, but each of us has seen the brilliant effect of the administration of the serum in the individual cases which appeals to us more. I remember the enthusiasm

of my father, who practiced medicine during the time of the introduction of antitoxin. In like manner our workers became enthused over the fine results in the individual cases. We find that many of them who could not well afford it were willing to work for less pay because of the remarkable results that they saw before them. One of the members of this society once heard me discussing this subject. He evinced some interest and some mental reserve. Later he came out

TABLE 3.—FEBRUARY, 1919, CASES

Six hundred and twenty-one babies were born in Minneapolis during February, 1919. Of these, at the end of each month listed, the data are presented.

	Feb. 18, 1919	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919
Breast fed	520	493	418	362	326	260	188	116	77
Breast fed complemental	31	46	61	63	78	126	168	215	224
Total breast fed*	551	539	479	425	404	386	356	331	301
Artificially fed	...	4	21	38	44	57	77	88	91
Total under observation†	551	543	500	463	448	443	433	419	392
Artificially fed from birth	11	11	11	11	11	11	11	11	11
Baby died	20	23	23	24	25	26	28	28	28
Mother died	1	1	3	3	3	3	3	3	3
Refused to give information	0	0	1	1	1	2	2	2	2
Moved out of town	0	3	19	39	39	40	41	45	54
Cannot be traced	4	6	30	46	60	62	69	79	97
Out of town cases	34	34	24	34	34	34	34	34	34
	621	621	621	621	621	621	621	621	621

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 392 February babies still under observation Oct. 31, 1919	301	77+	22+
Of the 419 February babies still under observation Sept. 30, 1919	331	78+	21+
Of the 433 February babies still under observation Aug. 31, 1919	356	82+	17+
Of the 443 February babies still under observation July 31, 1919	386	87+	12+
Of the 448 February babies still under observation June 30, 1919	404	90+	9+
Of the 463 February babies still under observation May 31, 1919	425	91+	7+
Of the 500 February babies still under observation April 30, 1919	479	95+	4+
Of the 543 February babies still under observation March 31, 1919	539	99+	¼+

* Fifty-four mothers of February babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increaase the milk supply.

† Feb. 28, 1919, 551 of the babies born in February were under observation. Oct. 31, 1919, 392 of these babiees were still under observation, 159 of the 551 babies under observation Feb. 28, 1919, having been dropped for the following reasons: baby died, 8 cases; mother died, 2 cases; refused to give information, 2 cases; moved out of town, 54 cases; cannot be traced, 93 cases.

to see us and I sent him out into the field with a nurse, keeping away myself. He saw two cases and ceased to be skeptical about maintenance of breast feeding and was wholly convinced.

We wish now to supplement this study with one of rural conditions in the state.

Through the members of our staff who are sent out on our rural clinics, we get reports from certain districts in which rickets is very

TABLE 4.—MARCH, 1919, CASES

Seven hundred and ninety-nine babies born in Minneapolis during March, 1919. Of these, at the end of each month listed, the data are presented.

	March 31, 1919	April 30, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919
Breast fed	615	541	470	429	377	339	234	130	62
Breast fed complemental	30	52	78	74	88	115	181	261	273
Total breast fed*	645	593	548	503	465	454	415	391	335
Artificially fed	...	41	58	74	87	96	102	119	132
Total under observation†	645	634	606	577	552	550	517	510	467
Artificially fed from birth	25	25	25	25	25	25	25	25	25
Baby died	20	29	30	32	32	32	35	35	35
Mother died	5	5	5	5	5	5	5	5	5
Refused to give information	1	1	1	1	1	1	1	1	1
Moved out of town	15	16	25	39	49	50	62	67	90
Cannot be traced	25	26	44	57	72	73	91	93	113
Out of town cases	63	63	63	63	63	63	63	63	63
	799	799	799	799	799	799	799	799	799

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 467 March babies still under observation November 30, 1919	335	71+	28+
Of the 510 March babies still under observation Oct. 31, 1919	391	76+	23+
Of the 517 March babies still under observation Sept. 30, 1919	415	80+	19+
Of the 550 March babies still under observation Aug. 31, 1919	454	82+	17+
Of the 552 March babies still under observation July 31, 1919	465	84+	15+
Of the 577 March babies still under observation June 30, 1919	503	87+	12+
Of the 606 March babies still under observation May 31, 1919	548	90+	9+
Of the 643 March babies still under observation April 30, 1919	593	93+	6+

* Eighty-three mothers of March babies were given special attention and taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

† March 31, 1919, 645 of the babies born in March were under observation. Nov. 30, 1919, 467 of these babies still were under observation, 178 of the 645 babies under observation March 31, 1919, having been dropped for the following reasons: baby died, 15 cases; moved out of town, 75 cases; cannot be traced, 88 cases.

common. In these neighborhoods infants are weaned for insufficient reasons. Fortunately, most of the children in the territory covered by our rural clinics, are breast fed. The study of breast feeding in smaller towns and rural districts should be very interesting, and should be made through the physicians as in Minneapolis. The conditions in certain other cities of large and smaller size and the same size over the country should be determined. Minneapolis has a low infant

TABLE 5.—APRIL, 1919, CASES

Seven hundred and nineteen babies born in Minneapolis during April, 1919. Of these, at the end of each month listed, the data are given.

	April 20, 1919	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919	Dec. 31, 1919
Breast fed	599	573	486	436	386	312	185	93	35
Breast fed complemental	17	27	56	70	93	134	225	221	224
Total breast fed*	616	600	542	506	479	446	410	314	259
Artificially fed	...	8	22	30	47	60	74	89	128
Total under observation†	616	608	564	536	526	506	484	403	387
Artificially fed from birth	7	7	7	7	7	7	7	7	7
Baby died	19	25	25	26	27	27	28	28	29
Mother died	1	1	2	2	2	2	2	2	2
Refused to give information	0	0	0	0	0	0	0	0	0
Moved out of town	8	9	35	48	53	62	67	70	71
Cannot be traced	15	16	33	47	51	62	77	155	169
Out of town cases	53	53	53	53	53	53	53	53	53
	719	719	719	719	719	719	719	719	719

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 387 April babies still under observation Dec. 31, 1919	259	66+	33+
Of the 403 April babies still under observation Nov. 30, 1919	314	77+	22+
Of the 484 April babies still under observation Oct. 31, 1919	410	84+	15+
Of the 506 April babies still under observation Sept. 30, 1919	446	88+	11+
Of the 526 April babies still under observation Aug. 31, 1919	479	91+	8+
Of the 536 April babies still under observation July 31, 1919	506	94+	5+
Of the 564 April babies still under observation June 30, 1919	542	96+	3+
Of the 608 April babies still under observation May 31, 1919	600	98+	1+

* Sixty mothers of April babies were taught expression of milk from the breast in order to stimulate the breasts and thereby increase the milk supply.

† April 30, 1919, we had 616 of the babies born in April under observation. Dec. 31, 1919, we had 387 of these babies still under observation, 229 of the 616 babies under observation April 30, 1919, having been dropped for the following reasons: baby died, 10 cases; mother died, 2 cases; moved out of town, 63 cases; cannot be traced, 154 cases.

TABLE 6.—MAY, 1919, CASES

Six hundred and fifty-seven babies born in Minneapolis during May, 1919. Of these, at the end of each month listed, the data are shown.

	May 31, 1919	June 30, 1919	July 31, 1919	Aug. 31, 1919	Sept. 30, 1919	Oct. 31, 1919	Nov. 30, 1919	Dec. 31, 1919	Jan. 31, 1920
Breast fed	506	446	363	301	266	221	164	87	66
Breast fed complemental	32	56	66	59	56	90	103	164	181
Total breast fed*	538	502	429	360	322	311	267	251	247
Artificially fed	...	16	54	74	88	90	107	111	114
Total under observation†	538	518	483	434	410	401	374	362	361
Artificially fed from birth	11	11	11	11	11	11	11	11	11
Baby died	17	22	22	24	24	25	26	26	26
Mother died	2	2	2	2	2	2	2	2	2
Refused to give information	0	0	0	0	0	0	0	0	0
Moved out of town	7	9	19	32	53	56	56	59	59
Cannot be traced	30	43	68	102	105	110	136	145	146
Out of town cases	52	52	52	52	52	52	52	52	52
	657	657	657	657	657	657	657	657	657

RESULT

	Breast Fed		Percentage on Artificial Food
	Number	Per Cent.	
Of the 361 May babies still under observation Jan. 31, 1920	247	68+	31+
Of the 362 May babies still under observation Dec. 31, 1919	251	69+	30+
Of the 374 May babies still under observation Nov. 30, 1919	267	71+	28+
Of the 401 May babies still under observation Oct. 31, 1919	311	77+	22+
Of the 410 May babies still under observation Sept. 30, 1919	322	78+	21+
Of the 434 May babies still under observation Aug. 31, 1919	360	82+	17+
Of the 483 May babies still under observation July 31, 1919	429	88+	11+
Of the 518 May babies still under observation June 30, 1919	502	96+	3+

* Forty-five mothers of May babies were taught expression of milk from the breasts in order to stimulate the breasts and thereby increase the milk supply.

† May 31, 1919, 538 of the babies born in May were under observation. Jan. 31, 1920, 361 of these babies still were under observation, 177 of the 538 babies under observation May 31, 1919, having been dropped for the following reasons: baby died, 9 cases; mother died, 52 cases; cannot be traced, 116 cases.

mortality for a city of its size. However, for the first year of the application of this work, the mortality dropped definitely. This may be entirely coincident, but I do not believe that it is.

DISCUSSION

DR. MCCLANAHAN: We in Nebraska look to Minneapolis for inspiration. We have been aware of the splendid work going on there for the past year. Dr. Sedgwick has given us a wonderful report. I wish to come to the defense of the mothers. It may be remembered that I read a paper on breast feeding

based on data obtained from 400 mothers. The question was aked, "Why did you wean your child?" and 385 said "because the doctor advised me to do so." It seems to me that we must do missionary work among the doctors. We have several young men here and I think we must attack the problem through them and urge them to preach the doctrine to other physicians in their community. The mothers are mostly willing to nurse their children if they are not advised to the contrary.

Two years ago I read a paper on the relative mortality and morbidity of breast fed and bottle fed babies and I showed that the morbidity of breast fed infants was less than that of bottle fed babies, based upon reports from prominent physicians over the country.

DR. TAYLOR: I believe Dr. Sedgwick has reported on this subject before national societies only during the last two or three years, but he has been doing this work and preaching this doctrine for a much longer time. I am under the impression that among many pediatrists a large proportion of their work has to do with the artificial feeding of infants; in our private practice that is a very small proportion of our work, as most of our younger babies are breast fed.

DR. KERLEY: It would be interesting if we could know the condition and weights of these breast fed infants at various ages. It is a question whether the infants nursed entirely for nine months do better than those nursed for three or four months. It would also be interesting to know the weight of infants nursed entirely nine months in comparison with those in which there has been earlier weaning followed by bottle feeding, or in which the breast feeding had been supplemented by the bottle.

DR. HOOBLER: The expression of mothers' milk has proved very satisfactory in connection with the establishment of our wet nursing bureau in Detroit. During one year several years ago 67,000 ounces of mothers' milk was expressed and distributed throughout the city to both the worthy poor and, as Dr. Sedgwick has said, the worthy rich. This year about 60,000 ounces of mothers' milk have been obtained in this way. It may be of interest to know that this method of expressing the milk that Dr. Sedgwick described has been used with very satisfactory results. The breasts have been able to produce larger and larger quantities. The opinion was expressed here several years ago that the distribution of mothers' milk might be put on a commercial basis and this we have done successfully. Many mothers receive adequate incomes from the sale of their milk at ten cents an ounce while it is given to the worthy poor for nothing, and to those who can pay it a charge of from 15 to 25 cents per ounce is made.

DR. GERSTENBERGER: There is no one thing that has reduced infant mortality more than the promotion of breast feeding. I should like to ask whether in the figures that appear on the first page of this report infants receiving breast milk part of the time were included or only those entirely breast fed.

How much does it cost to keep a staff going to do this work?

DR. FIFE: What were the intervals between feedings in the large proportion of these mothers?

DR. SMITH: We all agree as to the desirability of breast feeding and Dr. Sedgwick is to be congratulated on his results. It is a question, however, whether the expression of the milk has not been overestimated, and whether the good results are not due to awakening the attention of mothers to the advantages of breast feeding. Having expression of such for an incentive, breast feeding may be much more used than before.

DR. SEDGWICK: Dr. Porter speaks of the community being Scandinavian. That is true, and they are nursing their babies well and getting good results, but this is also true of others as the records show. The question has been asked whether we used complemental feeding. We used both complemental mixed feeding and full breast feeding. We do not know the exact weights of these babies all through the period of nursing, as that was too big an undertaking for us. As to what we advise mothers with asthenia and anemia, they are referred to their physicians. We have only one routine contraindication: open tuberculosis. As Dr. McClanahan says the mothers are not so much to blame for discontinuing the nursing. The doctor is often at fault. There may be a few cases of overstimulation, but they are very few in comparison with the ones that are understimulated, and therefore this piece of work did not lay stress on them. With reference to the interval, we have encouraged but not insisted on, four hour feeding, and four hour expression of both breasts of necessity. One of the greatest mistakes that is often made is that of alternating the breasts every four hours, that means that each breast is only stimulated every eight hours. Often this is not sufficient and both breasts should be expressed every four hours.

As to the types of diet, our directions have been very simple. We tell the mother she may have anything to eat that her husband should have. She needs a few more calories, however. An enormous amount of fluid is not as necessary or as important as continued stimulation. As to the cost of the work, we have two or three nurses and an office force, a stenographer and someone at the telephone. We spent $6,000 and we have now turned the work over to the Infant Welfare Association and they are doing it for $4,000 a year. Any one not doing the work in connection with that of another association would probably need a little more. I would like to stress the fact that we are very careful not to allow a child to be underfed, and we advise complemental feeding when necessary.

THE DIAGNOSIS AND PROGNOSIS OF TUBERCULOSIS IN INFANCY

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AND
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In 1914, under the stimulus of the ability to examine postmortem material in a large percentage of fatal cases at the Infants' Hospital, we began a detailed study of tuberculosis in the first two years of life. This study while, perhaps, not disclosing anything very startlingly new, has given results which may be of value in emphasizing certain peculiarities of the disease at this period of life, and which have the advantage of being based on a series of necropsies on children under 2 years of age which is larger than any we have been able to find in the literature, at least in American literature. The conclusions presented in this paper are based on a series of 374 cases in which a clinical diagnosis of tuberculosis was made in the wards of the Infants' Hospital, and on a series of 138 necropsies in which lesions of tuberculosis were found.

HUMAN AND BOVINE TUBERCULOSIS

The first question investigated was that of the relative preponderance of human and bovine tuberculosis in the babies found to be tuberculous at the hospital. This question was of interest because, in opposition to European authorities, many American authorities appeared to hold the opinion and to be teaching that tuberculous infection in the first two years of life was predominantly of bovine origin, conveyed through the medium of contaminated milk. Our results, which have been published, and which have only been confirmed by a larger series, showed that in an overwhelming preponderance of cases the infection was of human origin, conveyed in the ordinary manner of a contact infection. The second question was the closely connected one of the character of the primary lesion in the tuberculous infant. Here, again, many American authorities

maintained that the usual primary lesion is in the lymph nodes, this idea having arisen from the fact that the lymph node lesion is the most conspicuous lesion at the postmortem. Our results confirmed the view of Albrecht, Gohn and other European observers, that the tubercle bacillus does not pass through the mucous membrane to the lymph nodes without a trace, but causes a lesion of the mucous membrane at the portal of entry, which is the true primary lesion of the disease. Further necropsy statistics have only confirmed the results published in 1916. The fact that the primary lesion cannot be found in a few cases is not very significant evidence against this view, because the difficulty of finding the pulmonary lesion is so great that it is probable that it must be overlooked in a certain number of cases.

There are three portals of entry, the lung, the intestine, and the tonsils, and whenever infection occurs in the first two years of life, the primary lesion should be found at one of these points. There is always an associated tuberculous lesion in the regional lymph nodes draining the area of the primary lesion. In the great majority of our cases, more than 90 per cent., the primary lesion was found in the lung, with associated lesions of the tracheobronchial lymph nodes.

DIAGNOSIS OF TUBERCULOSIS

Our attention was next turned to the question of the diagnosis of tuberculosis in the first two years of life. The frequency with which there was found postmortem a tuberculous infection not suspected during life suggested the imperfection of a diagnostic method confined to mere routine examination of the lungs for evidences of consolidation. The incidence of tuberculosis at necropsy is placed by Hamburger at 23 per cent. in babies 1 year old, and at 40 per cent. in babies 2 years old. These figures probably have wide variations according to locality. In our series of 661 consecutive necropsies in children under 2 years, 138, or 20 per cent., showed tuberculous lesions. This frequency suggests how often the presence of the disease is overlooked clinically.

THREE STAGES OF TUBERCULOSIS

Hamburger divides tuberculosis into three stages, primary, secondary, and tertiary—the primary stage being represented by the primary lesion and the associated lymph node involvement; the secondary stage being represented by all the lesions produced by the

further invasion of the body by the tubercle bacillus, and the tertiary stage being represented by the chronic destructive lesions, such as the bone and joint tuberculosis of later childhood, and the phthisis of adult life. We believe that this division into stages is not only advantageous but actually essential in the study of infantile tuberculosis.

Every case in the entire series, both clinically and at necropsy, fell clearly and definitely into either the primary or the secondary stage as described by Hamburger. The cases in the primary stage showed clinically an absence of any evidence of the secondary lesions due to invasion, and pathologically lesions confined to the portal of entry and the regional lymph nodes. The cases in the secondary stage for the most part showed clinically the well known disease pictures of tuberculous bronchopneumonia, or tuberculous meningitis and pathologically a variety of lesions dependent on the route of invasion taken by the tubercle bacillus in advancing beyond the circumscribed limits of the primary stage. Invasion by direct extension from the lung gave tuberculous pleurisy. Invasion from the lung through the gastro-enteric tract gave secondary tuberculous ileocolitis, tuberculous peritonitis and tuberculosis of the mesenteric lymph nodes. Invasion through the air passages gave tuberculous bronchopneumonia. Invasion through the blood gave miliary tuberculosis and tuberculous meningitis. There was but one case in the tertiary stage, which apparently does not have to be considered in infantile tuberculosis.

In looking back over a series of records made before the beginning of the investigation which is the basis of this paper, we were impressed by the fact that the clinical diagnosis of tuberculosis in infancy was based on one of two classes of evidence. The first was the existence of some form of easily recognized clinical tuberculosis, such as tuberculous meningitis, tuberculous peritonitis, or tuberculous pleurisy. The second was the finding in the lung of evidences of chronic consolidation, with such confirmatory evidence as an up and down temperature curve, wasting and, perhaps, a positive von Pirquet reaction. The first class of cases are obviously of the secondary stage of the disease. In the second class of cases, those with evidence of pulmonary consolidation, the clinical diagnosis was in some instances "chronic pulmonary tuberculosis," in other instances "tuberculous bronchopneumonia," the differentiation between these two diagnoses depending on the acuteness of the case, the extent of lung involvement and the

rapidity of the respiration. Yet in looking over our series of 138 necropsies, we found that if we had based our clinical diagnoses on the above evidence, the diagnosis would not have been confirmed by the postmortem findings. With a few exceptions, all the cases showing during life evidence of pulmonary consolidation, showed postmortem tuberculous bronchopneumonia. The acuteness of the case, the extent of lung involvement, and the rapidity of the respiration had no apparent bearing on the diagnosis of tuberculous bronchopneumonia. There were a few cases in which the primary lung focus had grown large enough to produce signs of consolidation, and postmortem an appearance resembling the chronic pulmonary tuberculosis of adult resembled the excellent description of Gohn, and was too small to produce any clinical signs of pulmonary consolidation. The signs of consolidation when due to tuberculosis were produced by a tuberculous bronchopneumonia. Therefore, it appears that the diagnosis of tuberculosis, when based on the two classes of evidence described above, is really *based on the existence of the secondary stage of the disease,* because tuberculous meningitis, peritonitis, pleurisy and bronchopneumonia are all secondary lesions. This means that in the series of records made before the beginning of the detailed investigation, the diagnosis was only made when the secondary stage had been reached. Meanwhile, necropsies made during the same period every now and then disclosed cases in which no clinical diagnosis of tuberculosis had been made, but which postmortem showed only the lesions of the primary stage. It thus appeared that the diagnosis of tuberculosis in infancy in the primary stage was extremely difficult to make under ordinary routine methods of examination.

A study of our necropsy records taken from the period previous to the beginning of the detailed investigation also disclosed another difficulty. It appeared that the existence of chronic signs of pulmonary consolidation, even when associated with an up and down temperature curve and loss of weight, did not warrant a positive diagnosis of tuberculous bronchopneumonia. In many of these cases there was a chronic or unresolved bronchopneumonia, due to another cause, and showing no tuberculous tissue changes. It appeared, therefore, that even when signs of pulmonary consolidation are present, the diagnosis of tuberculosis must depend on more than the ordinary methods of examination. It is only when such definitely recognizable secondary lesions as meningitis or peritonitis are present, that the diagnosis can be made easily.

METHOD OF EXAMINATION

As a result of these observations, the following methods were adopted as a routine in the examination of the babies admitted to the hospital: The lungs were examined not only for signs of consolidation, but also for signs of enlargement of the tracheobronchial lymph nodes. The signs specially looked for were interscapular dulness, prolongation downward of the normal cervical dulness, and d'Espine's sign. The von Pirquet cutaneous reaction was tested, and repeated at intervals. In all cases which showed signs of pulmonary consolidation, or of bronchial lymph node enlargement, or which gave a positive von Pirquet reaction, or in which there was any other reason to suspect tuberculosis, such as exposure or unexplained loss of weight, a roentgenogram of the chest was taken. It proved impossible to carry out this method of investigation as thoroughly as we could wish. A certain number of babies included in the series died or were taken home before the von Pirquet reaction could be performed or interpreted. There were also many deficiencies in the records of the examination for signs of tracheobronchial lymph node enlargement. In the same way, many babies escaped without having a roentgenogram taken. Also, in a certain number of cases, the diagnosis of tuberculosis was plain from the lumbar puncture or some other form of evidence, and the collection of diagnostic evidence for statistical purposes was postponed until too late. With whatever evidence was obtained as a basis, a decision was made as to the presence or absence of tuberculosis. After committing ourselves, the postmortem findings were carefully studied in every case in which a necropsy was performed, and the after history was followed in as many as possible of the patients discharged from the hospital with the diagnosis of tuberculosis. We learned a great deal from this procedure, owing to the number of necropsies which were available. It is what we learned that we shall endeavor to present.

Table 1 is an analysis of the series with reference to the correctness of the diagsosis made under the methods employed.

The series shows, as a first point of interest, the frequency of clinical tuberculosis in hospital patients under 2 years of age. In 12 per cent. of all our admissions a clinical diagnosis of tuberculosis was made, and in 9 per cent. of all admissions this diagnosis was confirmed. The relative frequency of tuberculosis at necropsy, 20

per cent., is, of course, higher than the clinical frequency, on account of the tendency of the disease to end fatally in the first two years of life.

TABLE 1.—ANALYSIS OF 374 CASES

	Cases
Diagnosis of tuberculosis made	374
Total admissions to hospital in same period	3,100
Diagnosis confirmed	291
Diagnosis confirmed by necropsy	129
Total necropsies in same period	661
Diagnosis confirmed by subsequent clinical developments	153
Diagnosis remained unconfirmed	78
Diagnosis contradicted by necropsy findings	5
Diagnosis not made clinically in cases found tuberculous at necropsy	9

CONFIRMATION OF THE DIAGNOSIS

The diagnosis of tuberculosis was considered as confirmed in two ways. One was the finding of tuberculous lesions at necropsy; the other was the presence or subsequent development of unmistakable clinical types of the disease. The types regarded as unmistakable were typical cases of tuberculous meningitis, peritonitis, pleurisy, or cervical adenitis, or cases showing such clearly tuberculous lesions as Pott's disease or dactylitis, or the clinical finding of tubercle bacilli. No case in which a diagnosis of tuberculous bronchopneumonia or chronic pulmonary tuberculosis was made was placed in this unmistakable group. This confirmation was obtained in some cases by the presence or development of an unmistakable type while the patient was still in the hospital, or the development of such a secondary type in the cases followed through our Social Service Department. Cases in which tubercle bacilli were found in the sputum or in discharging ears were included in this group. There were twenty cases in which tuberculids were found on the skin. The cases in which the diagnosis was confirmed by postmortem examination form the larger group and their number was the most encouraging feature in leading us to continue this method of clinical study. In the cases in which the diagnosis of tuberculosis remained unconfirmed, it was made on the same evidence as in the confirmed group, but in these cases either no necropsy was performed, or the patients were discharged from the hospital and after discharge either failed to develop any recognizable form of tuberculosis, or else could not be followed up properly.

The most interesting figures in the table are those in which the clinical diagnosis was contradicted by the necropsy findings, and those in which the necropsy revealed that the presence of the disease had not been shown by clinical methods. Unfortunately, we are unable, owing to deficiencies in the records, to present exact figures showing these same points in a series of cases investigated by older methods of examination. In looking over a long series of hospital records, however, we were impressed both by the frequency with which the diagnosis of tuberculosis was unconfirmed by necropsy or subsequent developments, and by the frequency with which the disease was not recognized clinically, but was discovered at the necropsy.

In analyzing our series, we were encouraged to note that the majority of the cases of mistaken diagnosis occurred in the earlier years of the investigation. This suggested that our ability to make a correct diagnosis was increasing from year to year. Such an increase came from practice in interpreting the clinical evidence, particularly in the recognition of the physical signs of tracheobronchial lymph node enlargement, and in the interpretation of roentgenograms. This practice could only be obtained by the constant comparison of clinical with postmortem findings, by which our diagnoses were checked up while the clinical evidence was still fresh in the memory. The cases of mistaken diagnosis in our series will be further analyzed in connection with the various forms of evidence on which the diagnosis of the disease was based.

Table 2 shows the series of cases analyzed with reference to the clinical diagnosis, and the presence or absence of the evidence through which the forms presenting difficulty in diagnosis are to be recognized.

It will be noted that in many cases the von Pirquet test, the examination of the chest for interscapular dulness and d'Espine's sign or the roentgenogram were negative. Nevertheless, in the second group, showing the presence or absence of these signs in forms of tuberculosis presenting difficulty of diagnosis, *a diagnosis of tuberculosis was not made in any case unless at least one of these three signs was positive.*

Table 3 shows the presence or absence of the same three signs, taken not with reference to the clinical diagnosis, but with reference to the confirmation of the diagnosis by necropsy or otherwise. Of course, in all the cases of tuberculous meningitis in the series the diagnosis was also confirmed by lumbar puncture.

TABLE 2.—ANALYSIS OF THE DIAGNOSTIC VALUE OF SPECIAL METHODS OF EXAMINATION WITH REFERENCE TO CLINICAL FINDINGS

A. Unmistakable Forms	Cases	Confirmation			Von Pirquet			D'Espine			Roentgen Ray		
		Necropsy	Clinical Development	Unconfirmed	+	0	?	+	0	?	+	0	?
Tuberculous meningitis	124	77	47	0	46	26	1	40	21	13	38	2	8
Tuberculous peritonitis	19	4	11	4	9	7	2	1	13	1	1	5	3
Tuberculous pleurisy	1	0	1	0	1	0	0	1	0	0	1	0	0
Tuberculous cervical adenitis	1	0	1	0	1	0	0	0	0	1	1	0	0
Bone and joint tuberculosis	1	0	1	0	1	0	0	1	0	0	0	0	1
Total	146	81	61	4	58	33	3	43	34	15	41	7	12
B. Forms Presenting Difficulty in Diagnosis:													
Chronic primary tuberculosis	135												
a. Pulmonary	126	2	58	66	76	37	7	71	12	53	68	8	18
b. Intestinal	9	2	2	5	3	2	0	0	9	0	1	8	0
Tuberculous bronchopneumonia	34	10	21	3	16	15	1	20	9	14	20	0	8
Miliary tuberculosis (without meningitis)	54	43	11	0	25	23	0	24	17	11	28	1	5
Total	223	57	92	74	120	77	8	115	47	78	117	17	31
Grand total	369	138	153	78	178	110	11	158	81	93	158	24	43

TABLE 3.—THE DIAGNOSTIC VALUE OF SPECIAL METHODS OF EXAMINATION WITH REFERENCE TO NECROPSY FINDINGS

	Cases	Von Pirquet			D'Espine			Roentgen Ray		
		+	0	?	+	0	?	+	0	?
A. Confirmation by necropsy	143	59	37	2	80	32	31	48	11	18
1. Primary lesions only	4	3	1	0	2	2	0			
a. Lung	2	1	1	0	2	0	0	1	0	1
b. Intestine	2	2	0	0	0	2	0	0	2	0
2. Secondary lesions found	125	53	30	0	74	22	29	44	9	15
3. Clinical diagnosis not made; necropsy showed primary lesions of tuberculosis	9	0	5	0	0	7	2	None made		
3. Clinical diagnosis of tuberculosis; necropsy failed to confirm	5	3	1	0	4	1	0	3	0	2
B. Confirmation by clinical developments	153	61	51	5	44	32	27	85	8	17
C. Clinical diagnosis unconfirmed	78	61	23	6	38	18	35	28	5	10
Total	374	181	111	11	162	82	93	161	24	45

DIAGNOSTIC VALUE OF TUBERCULIN TEST

The von Pirquet reaction was present in the majority of cases. Comparison of our results with necropsy findings would suggest that the reactions designated as "suspicious" or "doubtful," should in the infant be considered as positive for purposes of diagnosis. Nevertheless, the reaction was negative in a fairly large proportion of cases in which the diagnosis of tuberculosis was confirmed either by necropsy, or by the development of some unmistakable type of secondary lesion. We realized some years ago that we were not obtaining at the Infants' Hospital so large a proportion of positive von Pirquet reactions in patients proved to be tuberculous as were being reported by other observers. We obtained new strains of tuberculin, made sure that we were using a correct technic, and made every effort to obtain an increased proportion of positive reactions, without success. In cases which eventually proved to be tuberculous, either through necropsy or through the subsequent development of manifest tuberculosis, the percentage of negative reactions was forty-two. In the cases proved tuberculous at necropsy, the reaction was negative in 37 per cent. We can only account for the discrepancy between our figures and those of other observers by the fact that all our observations were made in children under 2 years of age, while those of other observers included older children. Tuberculous infants seem to be more likely to show a negative von Pirquet reaction than older children.

We used to think that the reaction was more likely to be negative in proportion to the acuteness of the process, but this is true only to a certain extent. It is true that we obtained the highest proportion of positive reactions in cases showing only evidence of the primary stage of the disease, and the lowest proportion in the cases diagnosed as tuberculous bronchopneumonia and acute miliary tuberculosis without meningitis. Nevertheless, tuberculous meningitis, which represents a very acute form of infection, gave a fairly high proportion of positive reactions. More important as a factor in producing a negative reaction appears to be the general physical condition of the infant. Tuberculous babies in fairly good physical condition gave a very high proportion of positive von Pirquet reactions, while babies with notable atrophy and anemia gave the highest proportion of negative reactions. We believe that the high proportion of negative von Pir-

quet reactions obtained in tuberculous infants under 2 years is to be explained by the frequency of marked atrophy and anemia, which prevents the showing of a positive test.

We must assume from our results that the presence of a negative von Pirquet in no way rules out the diagnosis of tuberculosis in an infant under 2 years of age. The diagnostic value of a positive von Pirquet reaction in the infant appears to be much greater. In only five cases in our series did the necropsy findings fail to confirm the clinical diagnosis of tuberculosis. In only three of these cases was the von Pirquet reaction recorded as positive. It is, therefore, safe to conclude that in an infant under 2 years of age, a diagnosis of tuberculosis with very little chance of error may be made when positive von Pirquet reaction is obtained.

DIAGNOSTIC VALUE OF SPECIAL PHYSICAL SIGNS

The examination of the chest for interscapular dulness and d'Espine's sign is important. When no dulness or bronchial breathing is obtained below the level of the second dorsal vertebra, the sign should be considered negative. When the level is the third dorsal vertebra, the sign should be considered as doubtful, and no conclusion can be based on these signs alone. When the dulness and bronchial breathing is found below the level of the third dorsal vertebra, the sign should be considered as positive in cases without signs of pulmonary consolidation, and a diagnosis of tracheobronchial lymph node enlargement, presumably tuberculous, may be made. When there are signs of consolidation of the lung, they often mask d'Espine's sign and interscapular dulness, and caution must be exercised. Tuberculosis should not be diagnosed without other evidence in these cases. In our series, this method of examination was positive in 48 per cent., doubtful in 27 per cent. and negative in 25 per cent. It was negative in 22 per cent. of the cases which came to necropsy. In the primary stage of the disease, our necropsy statistics suggest that a diagnosis of tuberculosis based on a positive d'Espine's sign or interscapular dulness, or both, will be right in the majority of cases. A negative finding does not rule out tuberculosis, and is of course always the rule in cases of primary intestinal tuberculosis.

DIAGNOSTIC VALUE OF ROENTGENOGRAMS

The examination of roentgenograms of the chest eventually proved to be the diagnostic method on which we placed the greatest reliance.

Practice in interpreting plates is necessary, and this can only be gained by the comparison of clinical conclusions with necropsy findings. It is necessary to know what tuberculosis lesions of the chest are shown and what are not shown in roentgenograms. Four lesions in the chest are characteristic of the tuberculosis of infancy. These are, first, primary lesions in the lung, second, the accompanying enlargement and caseation of the tracheobronchial lymph nodes, third, miliary tuberculosis of the lung and fourth, tuberculous bronchopneumonia.

The primary lesion of the lung is not shown in the roentgenograms; it is too small. There were only one or two cases in our series in which there was found at necropsy a primary lesion large enough to give a shadow on a photographic plate. The enlargement and caseation of the bronchial lymph nodes can be seen in the majority of roentgenograms. This appears as a definite and characteristic shadow at the hilus of the lung, but much practice is required in distinguishing this shadow from certain shadows found at the hilus in normal infants. Congenital pulmonary atelectasis and thymic enlargement occasionally lead to a mistaken diagnosis. Acute miliary tuberculosis of the lung does not show in roentgenograms in the majority of instances. In the earlier cases of our series we frequently made a diagnosis of acute miliary tuberculosis of the lungs when the plates showed a peculiar spotted appearance. In the majority of cases of this kind which came to necropsy, the postmortem finding was tuberculous bronchopneumonia. Nevertheless, there were in the series a few spotted plates which showed no bronchopneumonia but showed a miliary tuberculosis of the lung with the formation of large conglomerate tubercles. Finally, tuberculous bronchopneumonia invariably shows in roentgenograms. We shall have more to say about these plates in considering the diagnosis of this form of infantile tuberculosis.

Roentgenograms of the chest were positive in 70 per cent. of the observations made in our series; positive or suspicious in 89 per cent.; negative in 11 per cent. These figures show their great diagnostic value in tuberculosis of the first two years of life. Necropsy findings also suggested that most of the roentgenograms recorded as doubtful or suspicious should have been considered positive. Negative roentgenograms in cases which came to necropsy were recorded in only 14 per cent. We may, therefore, conclude that a diagnosis of tuberculosis may be made by any one practiced in interpreting roentgenograms

whenever the roentgenogram is positive for tracheobronchial lymph node enlargement. A negative plate, however, does not rule out tuberculosis.

DIAGNOSIS OF THE PRIMARY STAGE

In general, as far as the diagnosis of the primary stage of tuberculosis is concerned, the following conclusions appear to be warranted: A positive von Pirquet reaction is the only evidence pointing toward a primary intestinal infection, and the diagnosis of this form of the disease cannot be made unless either the von Pirquet is positive or the physician is fortunate enough to find tubercle bacilli in the stools. Primary intestinal tuberculosis is, however, very rare in comparison with a primary focus in the lung, and it is in the recognition of this latter condition that special methods of diagnosis are particularly needed. If either the von Pirquet reaction is positive or even suspicious, or if the roentgenogram of the chest shows the shadow characteristic of tracheobronchial lymph node enlargement, a diagnosis of tuberculosis primary in the lung may be made with a fair degree of certainty. If the sole evidence is a positive or even suspicious d'Espine's sign, or interscapular dulness, the diagnosis may be made with only a slight degree of probability. In all cases in which all three of these forms of evidence are absent, tuberculosis in the primary stage should not be diagnosed.

DIAGNOSIS OF THE SECONDARY STAGE

In cases of the secondary stage of the disease the diagnosis so frequently depends on ordinary clinical evidence that these methods of investigation are unnecessary. Tuberculous meningitis is recognized by lumbar puncture. Tuberculous peritonitis is usually comparatively easy of clinical recognition. Tuberculous pleurisy can generally be recognized by the examination of the fluid obtained by thoracentesis. In a certain number of cases the finding of tubercle bacilli in the sputum or in some discharge, as from the ear, will give the clew to the diagnosis. There are, however, two secondary forms of the disease in which the diagnosis is more difficult. These are tuberculous bronchopneumonia and general miliary tuberculosis involving the lung and abdominal organs but in which the brain is spared.

DIAGNOSIS OF TUBERCULOUS BRONCHOPNEUMONIA

The characteristic sign of tuberculous bronchopenumonia in the infant is the finding of evidence of pulmonary consolidation. In general,

these cases tend toward a rather chronic course, but some of them are fully as acute as ordinary cases of nontuberculous pneumonia. No very reliable conclusion can be drawn from the extent and distribution of the consolidation as shown by physical examination. It is important in all these cases to determine whether the consolidation is due to a tuberculous pneumonia or to a pneumonia from some other cause. For this purpose we must rely on the same general signs of tuberculosis as we have considered in connection with the primary stage of the disease, namely, the von Pirquet reaction, the examination of the chest for signs of tracheobronchial lymph node enlargement, and the results of roentgenograms of the chest.

Table 4 shows these diagnostic signs in the cases of our series in which a diagnosis of tuberculous bronchopneumonia was made and confirmed at necropsy by the findings.

TABLE 4.—DIAGNOSTIC SIGNS IN CASES SHOWING PHYSICAL SIGNS OF PULMONARY CONSOLIDATION

Necropsy Findings	Cases	Von Pirquet			D'Espine			Roentgen Ray		
		+	0	?	+	0	?	+	0	?
Tuberculous broncho-pneumonia	42	21	10	1	38	1	3	20	1	5
Chronic primary tuberculosis plus nontuberculous pneumonia	4	?	0	0	2	1	1	1	0	3
Nontuberculous pneumonia without primary tuberculous lesions	5	3	1	0	4	1	0	3	0	2

It appears from the table that the von Pirquet reaction, the d'Espine's sign and interscapular dulness, or the roentgenograms gave the correct clew in forty-two cases. There were four cases in the series in which these signs only established a diagnosis of tuberculosis in the primary stage, the signs of pulmonary consolidation being due to a nontuberculous pneumonia. The remaining five cases are those in which a mistaken diagnosis was made. They showed at necropsy nontuberculous pneumonia without any lesions characteristic of the primary stage of tuberculosis. We may conclude from these statistics that in the majority of cases showing pulmonary consolidation, in which either the von Pirquet reaction or the roentgen ray is positive, the correct diagnosis is tuberculous bronchopneumonia. In a few cases, however, the diagnosis of tuberculosis will either be wrong, or else

there will be a combination of the primary stage of tuberculosis with a nontuberculous pneumonia. Roentgenograms will usually permit the observer to distinguish between tuberculous and nontuberculous pneumonia. In the tuberculous form the shadows are much more distinct and sharply outlined. Many plates show the characteristic speckled or spotted appearance which is never seen in nontuberculous pneumonia. When there are large areas of consolidation the shadows are usually much more dense than in nontuberculous pneumonia. It should be remembered, however, that occasionally a speckled or spotted plate means acute miliary tuberculosis of the lung with conglomerate tubercle formation and without the lesion of pneumonia . Such cases may, however, be recognized through the absence of signs of consolidation of the lung on auscultation and percussion. As far as the diagnosis of acute miliary tuberculosis without meningitis is concerned, there is nothing in the physical examination particularly characteristic of this lesion. General miliary tuberculosis may be suspected when fever is constantly high and emaciation extremely rapid. But in most of these cases the diagnosis of tuberculosis depends on the same evidence as is used in the recognition of the primary stage of the disease.

PROGNOSIS OF TUBERCULOSIS IN INFANCY

The analysis of the outcome of the disease to date in the cases in our series as shown by the hospital mortality and the subsequent mortality or present condition of the cases discharged from the hospital, is interesting as bearing on the prognosis of tuberculous infection when acquired during the first two years of life. This is shown in Table 5.

TABLE 5.—OUTCOME IN 369 CASES DIAGNOSED AS TUBERCULOSIS

	Cases
Died in hospital	194
Discharged living	175
Present condition unknown	50
Present condition known	125
Died after discharge	82
Alive and well	43

The mortality in the hospital was as high as 53 per cent. This, of course, does not give any accurate idea of the fatality of tuberculous infection in the first two years of life, because infants who seek hospital treatment are apt to show the more serious forms of the disease. It does suggest, however, the great prevalence of acute and fatal forms of the disease in the first two years of life.

The after history of the patients discharged from the hospital is still more significant as showing the importance of tuberculosis as a cause of death in infants. Of these 175 cases, we were unable to find or to obtain recent reports from fifty patients. Among the remaining 125 patients, eighty-two died after discharge from the hospital, so that the subsequent mortality was 66 per cent. and only forty-three patients of the original series of 369 are known to be alive at the present day. If the same proportion held among the cases lost as among those which could be followed, the figures for the series of 369 cases would be, living 60, died 309, a mortality of 83 per cent.

TABLE 6.—DIAGNOSIS AT DISCHARGE AND FINAL OUTCOME IN 175 CASES

	Cases	Living	Died	Lost
Primary stage	123	38	43	42
Tuberculous meningitis	14	0	14	0
Tuberculous bronchopneumonia	14	1	11	2
Tuberculous peritonitis	14	0	8	6
General miliary tuberculosis	7	1	6	0
Tuberculous cervical adenitis	1	1	0	0
Tuberculous pleurisy	1	1	0	0
Bone and joint tuberculosis	1	1	0	0
Total	175	43	82	50

Of the patients who died in the hospital, the cause of death in 188 was the existence or development of some severe form of the secondary stage of the disease. Of these secondary forms, tuberculous meningitis was the most common, tuberculous bronchopneumonia standing next in frequency. (Miliary tuberculosis without meningitis was a rare clinical diagnosis, but was the most common lesion found at necropsy, being present in almost every case of tuberculous meningitis, in many cases of tuberculous pneumonia, and occasionally being the only secondary lesion.) In the remaining six cases, only the lesions of the primary stage were found, and to these may be added the nine cases in which the diagnosis was not made during life, which also showed only lesions of the primary stage. In these thirteen cases, the tuberculosis could only be considered a contributing cause of death, as all the patients were admitted to the hospital for functional gastro-intestinal disease, and their clinical course was that of fatal cases of that character.

Of the patients discharged from the hospital, the diagnosis at the time of discharge with the present condition of the patient is shown by Table 6.

This table shows that the majority of the patients now living showed at the time of their discharge from the hospital only the primary stage of the disease. The patients in this stage who were followed to a subsequent fatal ending all developed a serious secondary form which was the cause of death. It is also an interesting fact that *this secondary form usually developed within a comparatively short time after discharge, usually within the period of infancy, that is, before the end of the second year of life.* As our investigation covered the years from 1914 to 1919, inclusive, most of the patients now living are well over the age of 2 years, and there have been very few instances of the later development of a fatal form of tuberculosis. It is to be noted also that the cases which we have been unable to follow through the Social Service Department were for the most part in the primary stage of the disease at the time of discharge. If in these cases a fatal form of tuberculosis had developed within a comparatively short time, the outcome would have been recorded before they were lost to view, and it is, therefore, probable that the majority of these patients are living, although we have no certain proof of this. Most of the survivors whom we have been able to follow have been examined recently and appeared to be in perfect health, but all who were discharged in the primary stage of the disease still show the same signs of tuberculosis as were present when the diagnosis was made in the hospital.

We may conclude from the subsequent history of these cases, that *the prognosis of infantile tuberculosis is best when the patient shows evidence that the disease has not advanced beyond the primary stage, but is still not good,* owing to the tendency of the infant to develop fatal forms of the secondary stage. This tendency is greatest in infancy, and grows less as the child grows older. This feature suggests that the infant has a very low resistance against widespread and serious invasion of the body by the tubercle bacillus, but as it grows older it shows a constantly increasing resistance against the more dangerous forms of the disease. It is tuberculous meningitis and tuberculous bronchopneumonia that are especially characteristic of infancy, while pleurisy, peritonitis, cervical adenitis, and bone-joint tuberculosis, all less fatal forms, are the ones associated with later childhood.

The figures from the forms of the secondary stage show that only tuberculous meningitis or general miliary tuberculosis are absolutely fatal. In all the other forms of tuberculosis there is a possibility of

recovery, but the prognosis is much worse than in the primary stage. In the first place, these types may be fatal in themselves, tuberculous bronchopneumonia being the most serious next to the miliary forms. Not only, however, is there this danger, but also in all these forms there is the same tendency toward the development of meningitis or miliary tuberculosis as was seen in the primary stages, this tendency being greatest in infancy.

If it were not for this tendency, characteristic of infancy, toward the development of severe secondary forms of tuberculosis, we would have little evidence of the value of our diagnostic methods in recognizing the disease while the patient was still in the primary stage. Comparatively few cases diagnosed as being in this stage of the disease came to necropsy; the majority left the hospital alive. But their subsequent histories and mortality substantiated the diagnosis so frequently, that we believe that the recognition of the primary stage of the disease can be made in most cases through the use of the von Pirquet reaction, roentgenograms, and careful examination for the physical signs of tracheobronchial lymph node enlargement. The importance of making the diagnosis in this stage is evident from the peculiarities of the prognosis of tuberculous infection acquired in infancy. This prognosis is bad. Would it be so bad if the presence of tuberculosis in the infant were recognized earlier, and proper treatment instituted as early as possible? This could only be done by means of a systematic and thorough examination of every infant with special reference to tuberculosis. We believe that the physician should consider the possibility of tuberculous infection in the case of every infant that comes under his care. That the infant shows no evidence of being sick should make no difference, for if the disease is in the primary stage, no symptoms suggesting tuberculosis are manifested, but the child will either seem well, or else present itself as a "feeding case," showing only symptoms of functional gastrointestinal disturbance.

We have heard the very harmful and meaningless word "pretuberculous" applied to infants. We have heard the term "latent" or "inactive" tuberculosis applied to infants with the implication that there was little or no danger. Physicians should recognize that an infant is either tuberculous or it is not. If there is one tubercle bacillus, or the smallest tuberculous lesion within the body, the infant is tuberculous. There is no "healed tuberculosis" in the infant. If the

tuberculous lesion is latent, inactive, it is better than if the infant had tuberculous meningitis, but the infant is none the less in danger. It is not difficult to make the von Pirquet test on every infant seen, nor to examine the back for interscapular dulness and d'Espine's sign. Often the diagnosis can be made without a roentgenogram, but one should be made in as many cases as possible.

We believe that if this procedure were more generally carried out, many more cases of infantile tuberculosis would be recognized while in the primary stage. Later we shall have some interesting statistics to present on the question of the contagiousness of tuberculosis, and the rôle of exposure in infantile tuberculosis. For the present, we will only say that we believe that every infant who has been exposed to an adult consumptive, is as certainly if not more certainly infected as would be a 10 year old school child similarly exposed to, let us say, scarlet fever. All children with a history of exposure should, for purposes of prognosis and treatment, be considered as in the primary stage of tuberculosis. There is so little provision near Boston for the proper treatment of tuberculous infants, that we cannot quote results, but we believe that with earlier recognition of tuberculosis in the infant and with the institution of appropriate treatment, there would be fewer cases seen of dangerous or fatal secondary stage forms, fewer deaths, fewer despairing mothers receiving the verdict which goes with tuberculous meningitis, and asking how such a thing could have occurred in a baby who has always seemed so well.

CONGENITAL UNDER-DEVELOPMENT OF THE RIGHT SIDE IN A THREE MONTHS OLD INFANT

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REPORT OF CASE

J. S., 3 months old, was brought to my office Dec. 11, 1919, by his mother because she had noticed a few days before that his left leg was much larger than his right.

Previous History.—Instrumental labor. Baby was apparently normal at birth. He has been fed exclusively on breast milk and has never been ill, and until a few days ago his mother has not noticed that the left side of his body, especially the left leg, was larger than the right.

Physical Examination.—Apparently perfectly nourished male child. Has been all his life and is now perfectly well. His only abnormality is the underdevelopment of the right side of the body, especially the right leg. The right leg is 10 inches long, the left leg 11 inches long, measured from the anterior superior spine to the internal malleolus. The right thigh, one inch above the knee, is 8¼ inches in circumference, the left thigh is 10 inches in circumference. The right foot, plantar surface, measured by placing the foot on a sheet of paper, is 3¾ inches, the left foot measured in the same way is 4 inches.

The right side of the chest, from the xyphoid process to the corresponding spinous process of the vertebrae, measures 8¼ inches. The left side of the chest, measured in the same way, is 8¾ inches.

The right femur is 1.8 inches shorter than the left. The right tibia is 1.2 inches shorter than the left.

March 23, 1920. Baby is now about 7 months of age. Has remained perfectly well and has continued to be nourished exclusively on breast milk. He weighs 20 pounds. The left side of his body is as well developed as that of any normal breast-fed baby of his age, but the whole right side of his body, although there has been a marked increase in development, still remains underdeveloped as compared with the left.

The left side of the baby's face is larger than the right. The left arm and hand are larger than the right. The most marked difference is in the size of the legs. The whole left leg is very much larger than the right. This is especially noticeable in the thighs. The left foot is several sizes larger than the right. It is also apparent that the left side of his chest is larger than the right. The baby is normally developed mentally. In standing the baby on his feet it is evident that he has more strength in his left than he has in his right leg. He apparently also has more strength in his left arm and hand than he has in his right, but this difference between the left and the right side is only comparative, as the baby uses his right arm and his right leg in an apparently normal

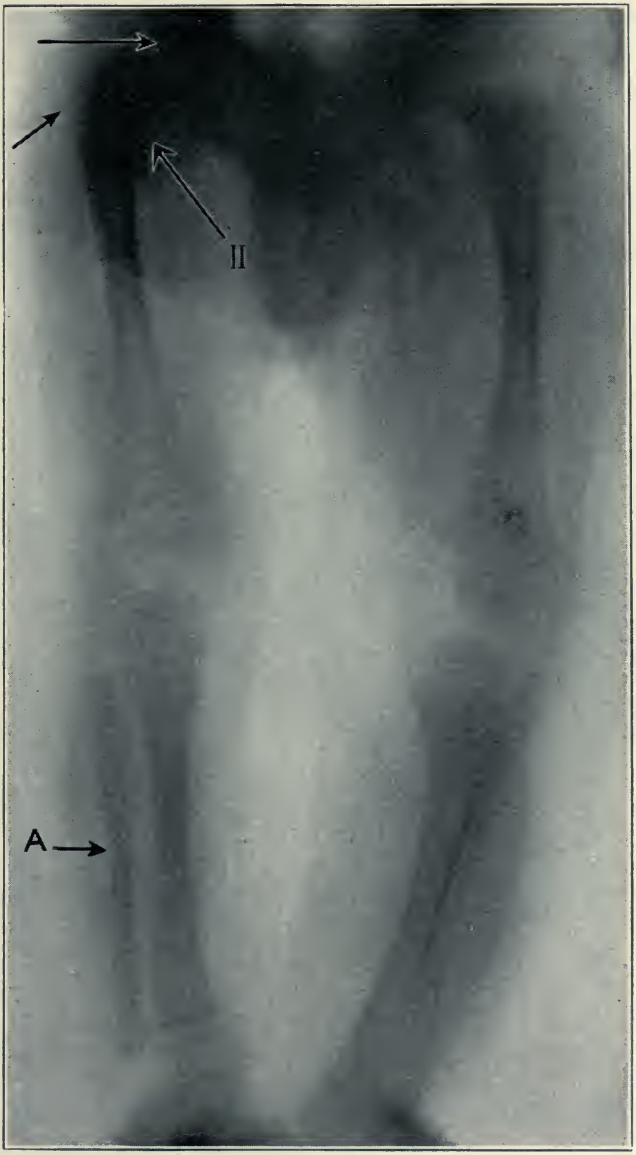

Fig. 1.—Underdeveloped tibia and fibula, right side (*A*) age 3 months.

way, and there is not the slightest evidence of paralysis of any kind. In fact, the mother believes that he has quite as good use of his right arm and leg as he has of his left.

Right leg now measures 12 inches; left leg, 13¼ inches; circumference right thigh, 9 inches; left thigh, 10½ inches; left foot, 4¾ inches long; right foot, 4¼ inches long.

Figures 1 and 2 show the underdevelopment of the bones of the right leg and the progress of development that has occurred in five months.

Fig. 2.—Age, 7 months. I. Underdeveloped epiphyseal ossification center. II. Lesser developed greater and lesser trochanter as compared with left side. III. Lesser transverse diameter of right femur as compared with left.

MALNUTRITION FROM UNDERFEEDING IN A CHILD TWO AND ONE-HALF YEARS OF AGE

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REPORT OF CASE

April 12, 1919, white male child, 2½ years of age, was referred to me by Dr. Alfred Freiberg. He was brought to my office in his father's arms because he could not walk.

The child was malnourished; from the time he was 8 months of age he had suffered more or less from intestinal fermentation, and for that reason had been underfed.

Five weeks ago he commenced to limp in his right leg, and the lower portion of the leg, especially about the ankle, became tender and swollen. This condition rapidly increased so that the child was unable to walk.

Previous History.—The mother nursed the child from birth until he was 8 months of age; at this time he was weaned and placed on modified milk. He soon developed a gastrointestinal fermentation, which has continued until the present time. To overcome this condition he was given skimmed certified milk and Mellins food. Soon after, orange juice was added to his diet. From the age of 14 months until the present time his diet has consisted almost exclusively of three pints of skimmed milk daily, beef juice, zwieback, rice and cream of wheat. He never could take oatmeal or eggs. The mother states that other foods were tried from time to time, but that any deviation from the above diet always produced loose, foamy and offensive stools, and even when taking the above named foods it was necessary to give him intestinal antiseptics, and at times bismuth in some form, to prevent loose bowel movements.

Six weeks ago he had an attack of influenza, which increased the intestinal disturbance, producing a slight cough and an elevation of temperature from time to time. These symptoms had continued up to the present time.

Physical Examination.—The child was rather poorly nourished. He was pale and anemic looking. He was rachitic; his chest, arms and legs were rather undeveloped; the rachitic rosary could be felt; his abdomen was very much distended (pot-belly), and there was a flaring of the lower portions of the ribs. The superficial lymph glands were not noticeably enlarged, except the posterior cervicals, which were slightly increased in size. The superficial veins of his face were quite noticeable. The urine was normal. The heart and lungs were normal. He had good movement of every portion of his body except his right leg, which, below the knee, was swollen and painful to the touch. The swelling and tenderness above the right ankle was quite marked. The right foot was held in marked valgus. The prepuce was irritated, red and swollen, and had been so for a number of months.

Blood Examination.—Hemoglobin, from 75 to 80 per cent.; red blood corpuscles, 4,730,000; leukocytes, 13,400; polymorphonuclears, 35 per cent.; small lymphocytes, 41 per cent.; large lymphocytes, 23 per cent.; mononuclears, 1 per cent.; eosinophils, 0 per cent.; basophils, 0 per cent.

Treatment.—A dose of castor oil was given, this to be repeated once a week, if necessary, to clear the intestinal canal of mucus. Three grains of saccharated carbonate of iron, and 1½ grains of iodonucleoids were given in a teaspoonful of maltine and hypophosphites three times a day after eating.

Diet: One quart of peptonized milk daily, rice, cream of wheat, baked potatoes, new peas and string beans. Vegetables to be well cooked, mashed and put through a colander.

April 17: A von Pirquet test was negative. An examination of the stool showed that the above foods were well digested; no parasites were found. On this date slightly cooked scraped beef was added to his diet.

April 22, 25 and 29: Examination of the stools showed fairly well formed intestinal discharges, with little or no evidences of undigested food.

April 29: A second von Pirquet was negative. At this time the child's general appearance was greatly improved. His pallor had begun to disappear. He had a good appetite, and with the aid of a small leather brace, prescribed by Dr. Albert Freiberg, he had begun to walk. The swelling and redness of the prepuce noted on his first visit quickly disappeared.

June 14: With the aid of his brace the child was walking fairly well. The swelling, pain and tenderness in his right leg and ankle, which began to improve almost at once after he was put under treatment, had now almost entirely disappeared. There was only a slight suggestion of puffiness above the ankle. The improvement in his general condition was very great; apart from his slight lameness and the abdominal distention, his appearance was that of a normal child.

The blood examination made at this time was as follows: hemoglobin, 90 per cent.; red blood corpuscles, 5,550,000; leukocytes, 8,200; polymorphonuclears, 30 per cent.; small lymphocytes, 34 per cent.; large lymphocytes, 22 per cent.; mononuclears, 9 per cent.; eosinophils, 3 per cent.; basophils, 2 per cent. This blood examination, as compared with the one made two months before, showed a marked increase in the hemoglobin percentage and in the number of red blood corpuscles. There was also a very marked decrease in the number of white blood corpuscles with a decrease in the relative percentage of lymphocytes.

At this time the boy was on the same medication prescribed above. The castor oil prescribed at his first visit was given only a few times. The iron, iodonucleoids and maltine, which he was still taking, was ordered continued throughout the summer. His food now consisted of one quart of peptonized milk daily, meat every day, either lamb, chicken or beef, almost all kinds of fresh vegetables, orange juice, apple sauce, cereals, bread and toast.

Dec. 29, 1919: He went through the summer without illness, except for a slight intestinal disturbance, which lasted for a few days. During the fall he had a cold once or twice, which did not disturb his digestion.

The boy today is apparently as well and strong as any child of his age. His skin is rosy, his body well formed. There is no longer any evidence of trouble in the right leg. He has perfect action of all parts of his body. He ran about and played "catcher" through my office with the activity of a normal boy. His mother, however, reports that he is not yet able to take milk in any form, except peptonized milk, of which he still continues to take a quart a day.

His diet at the present time, in addition to the peptonized milk, includes orange juice, cooked fruits, vegetables, cereals, bread, beef, lamb, chicken, and desserts containing egg, but raw milk and ice cream are still excluded from his diet.

Blood examination now shows: red blood corpuscles, 4,937,000; white blood corpuscles, 9,060; polymorphonuclears, 49 per cent.; small lymphocytes, 23 per cent.; large lymphocytes, 12 per cent.; mononuclears, 11 per cent.; eosinophils, 5 per cent.

On dismissing this patient I advised his mother to gradually discontinue the peptonized milk and add eggs to his diet.

From the time this boy came under my observation until his discharge, I was very much interested in his rapid progress toward recovery, and especially in the blood changes here recorded. On my first examination his previous history, his general appearance and the blood picture were strongly suggestive of tuberculosis, but I now believe that tuberculosis played no part in his malnutrition. I think that not only the blood changes but the whole clinical picture above recorded was due to malnutrition from intestinal fermentation and insufficient and improper food.

I also believe that the prompt recovery which resulted in this boy's case was largely brought about by the use of peptonized milk, which enabled him to take meat, vegetables, fruit and cereals without causing intestinal disturbance. I make this note because I feel that the prejudice among the profession against peptonized milk in the treatment of malnutrition is unjustified. It makes not only the giving of milk in many of these cases possible, but it also greatly increases the range of the child's digestive capacity for other foods.

THE MISUSE OF MILK

B. RAYMOND HOOBLER, M.D.

DETROIT

The value of milk as a food for adults and children has been exploited during the past few years to such an extent that its use is being much increased. This has inevitably led to many dietetic errors particularly in the group of children between the ages of 1 and 6 years. These errors may be classified as follows:

1. Prolonged use of milk as an exclusive article of diet.
2. Increased quantity of milk given with other foods.
3. The use of Jersey milk as particularly suitable for children.

Anyone who is constantly meeting the mothers of today must be impressed with the fact than they are being taught through the medium of the printed page and the billboards to regard milk as the one fundamental, indispensable, article of diet for children. The statements that milk contains "all the food elements in proper proportion," "rich in mineral salts," "furnishes vitamins," "each quart contains as many calories as a pound of beefsteak," while perfectly true in themselves do not constitute proof positive that milk should be fed in large quantities over long periods of time. Through the propaganda of the lay press and the advertising of the dairies many mothers, of themselves and frequently on the recommendation of their family physician, have kept their children on an exclusive milk diet up to the age of one and two years, or if not on an exclusive milk diet, so much milk has been given as to rob the child of an appetite for other foods. This is an easy error for the mother to commit since it is often difficult to break the bottle habit and to introduce spoon feeding. Furthermore, much more of the mother's time is required to prepare and feed the cereal, fruit and vegetables, which constitute a properly balanced diet. The child itself often shows a decided preference for the milk and an equal dislike for that which is offered to it in a spoon, the spoon being associated in the child's mind with something which tastes bad, castor oil, etc.

These difficulties connected with the feeding of foods other than milk, together with the inherent belief that milk is the best food, leads

the mother to continue an exclusive milk diet for a much longer period than is best for the child. It is not uncommon in a busy practice to find children kept on such a diet as long as eighteen months and even to two years. The picture which these children present at the end of such a period is well known—they are overweight, anemic, their tissues are flabby, they have a pasty appearance and often show symptoms of acute rickets.

Another group of children in which milk is misused are the children between the ages of 2 and 6 years. These children are allowed to eat at the family table and have a generous mixed diet, but in addition they are required by an overzealous mother, nurse or father to consume a quart of milk a day either with or between meals. Often this is no hardship, as the child is fond of milk. This inevitably leads to overfeeding, particularly with fat, and results in the child being in a constant state of alkali depletion with acetonuria. These are the children who are brought to us because of recurrent attacks of vomiting together with habitual constipation.

The removal of the excess of milk from the diet is usually all that is necessary to bring peace into the home where constant fear of recurrent attacks of vomiting has held sway, often for years.

Another fallacy which is prevalent in the lay mind is the belief that milk is good or bad for a child in proportion to the cream line on the milk bottle—the farther down the line is on the bottle, the better the milk. There is nothing which will play such havoc in nutrition as to attempt to bring up a family on Jersey or Guernsey milk. This is true particularly in the well-to-do families, who own their country estates, stocked with thoroughbred Jerseys or Guernseys, and to the people in small villages and in the country where the family cow happens to be of the high fat producing breed. City folks are not so subject to this menace since the average milk delivered is usually from herds, and the fat proportion is kept down for economic reasons. However, the propaganda distributed to the city people makes them wish that they could feed their children on Jersey milk. In Detroit the picture of the head of a Jersey cow is used as an emblem of the best milk for babies.

Milk may not only be used too long as an exclusive diet and in excessive quantities, but its nutritional value may be injured by boiling. The laity in many instances are being taught and rightly so that milk is an ideal breeding place for germs, and that the growth of these

germs may be inhibited by keeping the milk on ice, or if no ice is available the milk may be brought to the boiling point and kept covered. Through this teaching, and through the printed instructions accompanying certain patent baby foods, I believe the use of boiled milk is becoming more prevalent, and many injuries to nutrition occur. In some instances milk is boiled without realizing it. This may occur

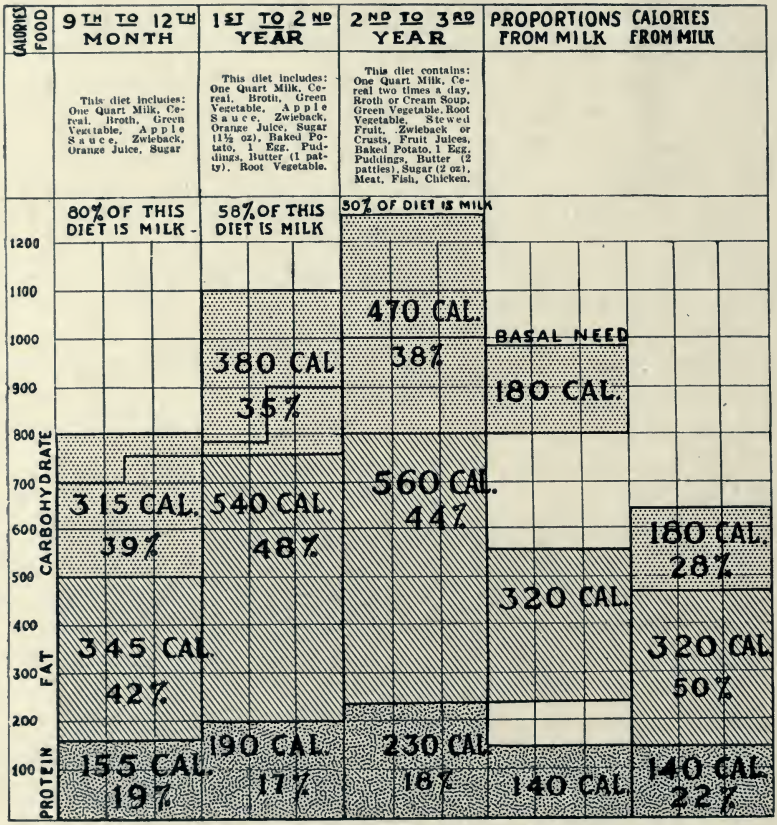
CALORIES
FOOD
9TH TO 12TH MONTH
1ST TO 2ND YEAR
2ND TO 3RD YEAR
PROPORTIONS CALORIES FROM MILK FROM MILK
This diet includes: One Quart Milk, Cereal, Broth, Green Vegetable, Apple Sauce, Zwieback, Orange Juice, Sugar
This diet includes: One Quart Milk, Cereal, Broth, Green Vegetable, Apple Sauce, Zwieback, Orange Juice, Sugar (1½ oz), Baked Potato, 1 Egg, Puddings, Butter (1 patty), Root Vegetable.
This diet contains: One Quart Milk, Cereal two times a day, Broth or Cream Soup, Green Vegetable, Root Vegetable, Stewed Fruit, Zwieback or Crusts, Fruit Juices, Baked Potato, 1 Egg, Puddings, Butter (2 patties), Sugar (2 oz), Meat, Fish, Chicken.
80% OF THIS DIET IS MILK
58% OF THIS DIET IS MILK
50% OF DIET IS MILK
1200
1100
1000
900
800
700
600
500
400
300
200
100
CARBOHYDRATE
FAT
PROTEIN
315 CAL. 39%
345 CAL. 42%
155 CAL. 19%
380 CAL. 35%
540 CAL. 48%
190 CAL. 17%
470 CAL. 38%
560 CAL. 44%
230 CAL. 18%
BASAL NEED
180 CAL.
320 CAL.
140 CAL.
180 CAL. 28%
320 CAL. 50%
140 CAL. 22%

Figure 1

in various ways, and only after careful search can the error be discovered. One such way is through the use of the electric bottle warmer. A certain bottle warmer provides only a depth of about 3 inches of water. This serves perfectly when only from 2 to 4 ounces

of milk are to be heated. Only the bottom 4 ounces of the bottle is in the water-bath and unless the bottle is constantly shaken, the bottom part must be brought to a boil in order when shaken to bring the top part to the correct temperature. Two instances of this error in overheating milk in this manner resulted in mild cases of tetany. Another method of overheating milk is by mixing the milk with the cereal water diluent while it is still boiling hot. A busy mother, anxious to complete the formula, will not wait until the cereal diluent is sufficiently cooled before adding the milk. A case of well developed scurvy was traced to this source.

I have constructed a chart showing how large a part of the caloric need is supplied when a quart of milk is given, and I have shown how a child may be overfed when given other foods in addition to the quart of milk. A large proportion of fat enters into the diet of these children. As soon as the use of butter is begun, the fat proportion rises rapidly. A small pat of butter represents a glass of milk. The chart shows the fundamental nutritional need as shown by Dubois and is indicated by the line marked "basal need." The calories are estimated from figures in the latest edition of Holt's book and from Irving Fisher's tables. Several years ago I presented before this society a study of the protein need of infants, based on calorimetric observations conducted under the direction of Prof. Graham Lusk. At that time the more limited use of milk was advocated, based on the facts adduced in those studies. Since that time, I have consistently adhered to the practice of feeding only sufficient milk to supply the protein need. This has led to the feeding of less milk than is usually recommended. Rarely does it seem necessary to feed more than 16 ounces of milk to an infant under 6 months of age, 20 ounces between 6 and 8 months and 24 ounces between 8 and 12 months. After 12 months, with the greatly increased spoon feeding, one pint a day fulfills the requirements. Infants thus fed are not fat, but their muscles are hard, their color is good and their weight is within normal limits.

Figure 1 shows the diets usually fed between 9 and 12 months, between 1 and 2 years and between 2 and 3 years which is the time when the child is under the strictest dietary supervision. This chart shows the relative proportion of the day's calories supplied by milk when one quart of it is fed, 80 per cent. being between 9 and 12 months old; 58 per cent. between 1 and 2 years, and 50 per cent. between 2 and 3 years. It also shows the relative proportion of the

different food elements fed when one quart of milk is ingested with other food. The fats proportion is relatively high and the carbohydrate relatively low. It also shows the amount of overfeeding above the basal need, which takes place when one quart of milk is fed, although often the child will change this by refusing the spoon feeding and will take only the milk, thus making a bad matter worse, since

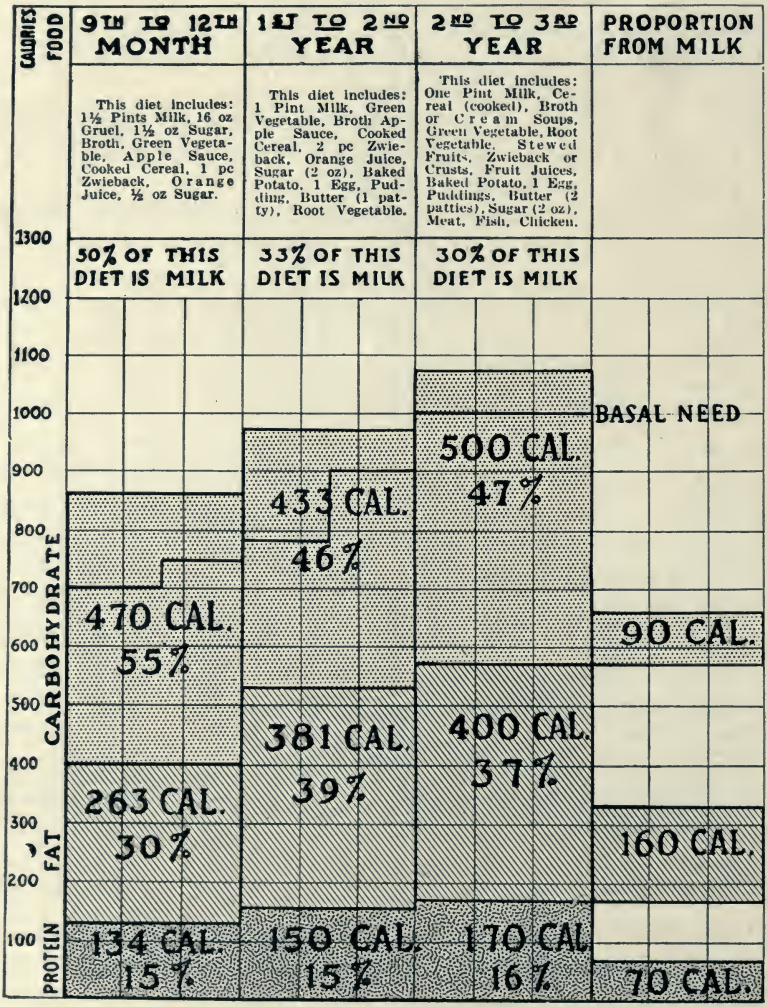
CALORIES
FOOD
9TH TO 12TH MONTH
1ST TO 2ND YEAR
2ND TO 3RD YEAR
PROPORTION FROM MILK
This diet includes: 1½ Pints Milk, 16 oz Gruel, 1½ oz Sugar, Broth, Green Vegetable, Apple Sauce, Cooked Cereal, 1 pc Zwieback, Orange Juice, ½ oz Sugar.
This diet includes: 1 Pint Milk, Green Vegetable, Broth Apple Sauce, Cooked Cereal, 2 pc Zwieback, Orange Juice, Sugar (2 oz), Baked Potato, 1 Egg, Pudding, Butter (1 patty), Root Vegetable.
This diet includes: One Pint Milk, Cereal (cooked), Broth or Cream Soups, Green Vegetable, Root Vegetable, Stewed Fruits, Zwieback or Crusts, Fruit Juices, Baked Potato, 1 Egg, Puddings, Butter (2 patties), Sugar (2 oz), Meat, Fish, Chicken.
50% OF THIS DIET IS MILK
33% OF THIS DIET IS MILK
30% OF THIS DIET IS MILK
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
CARBOHYDRATE
FAT
PROTEIN
470 CAL. 55%
263 CAL. 30%
134 CAL. 15%
433 CAL. 46%
381 CAL. 39%
150 CAL. 15%
500 CAL. 47%
400 CAL. 37%
170 CAL. 16%
BASAL NEED
90 CAL.
160 CAL.
70 CAL.

Figure 2

it robs the child of the minerals which should come to it in fresh fruits, vegetables and cereals, not to mention the vitamin and anti-scorbutic properties which these foods possess.

Figure 2 shows the caloric value and proportion of food elements when one pint of milk is fed daily from 1 to 3 years, together with approximately the same spoon feeding as in Figure 1. The total calories are reduced to within the normal requirements, thus preventing overfeeding. The proportions of fat and carbohydrate are nearly interchanged, thus giving the child ample carbohydrate calories to use up in activity. There is also a lowering of the protein proportion down to the maximum for growth and wear and tear.

Children fed diets shown in Figure 2 come up to the end of their third year with hard muscles and good color, and they are free from vomiting attacks, stupor accompanied by acetonuria so prevalent in children who have been fed according to Figure 1. These observations are not based on theoretic diets but are based on the actual régime of many children who have been brought through babyhood to their fourth year with not to exceed 24 ounces of milk between 9 and 12 months and not to exceed one pint daily after the first year. I recognize that all children cannot be fed in the same manner and that some cannot even take the minimum amount of milk recommended.

SUMMARY

The propaganda urging the feeding of a quart of milk a day is fallacious. When done it leads to (1), overfeeding; (2), an unbalanced ration; (3), unhealthy nutrition, and (4) frequent attacks of vomiting, with stupor accompanied by acetonuria.

DISCUSSION

DR. KERLEY: My views in this matter are in accord with Dr. Hoobler. After a child is 18 months old, I usually give milk only to the amount of one pint a day, provided the child can be adequately nourished otherwise. A large amount of milk consumed daily takes away the child's appetite and capacity for caring for other foods. Further, children who have been fed large quantities of milk are very apt to show a secondary anemia and faulty development.

DR. LADD: In feeding milk one ought to consider the use of butter. In the second, third and fourth years children begin to get butter, and the harmful effect attributed to milk may be due to the excessive use of butter fat given on the theory that the more butter the child eats the better. One reason why many of us have given a quart of milk daily, without serious consequences, to children two, three or four years of age is that we regulate with great care the amount of butter in the diet.

DR. HOLT: I dislike to have the impression go out that it is the opinion of the American Pediatric Society that too much milk is now being given to children. It is my own belief that at the present time children, as a rule, are getting far too little milk. Careful surveys which have been made in New York City show that, owing to the increased cost of milk, many families which were formerly taking two or three quarts a day are now taking only one quart or one pint, and in not a few cases no milk at all. It is undoubtedly true that children who eat a hearty meal and then drink one or two glasses of milk are usually getting too much food, and the disturbances of digestion which follow are due to over-feeding, although it is not uncommon to blame the milk as the cause. I fully appreciate the fact that milk is not a sufficient diet for children for the first two years and that a serious degree of anemia often results when milk is given as the sole diet or almost the sole diet for this period, as so often happens in children who have not been taught to take other food than that given from a bottle. Milk contains two very important essentials for growth. The first is calcium and the other is the fat-soluble vitamin. The other chief sources of calcium in the diet are eggs and green vegetables, of which spinach has the largest amount; but one good helping of spinach contains only about as much calcium as does one ounce of milk; and one egg only a little more than is in one ounce of milk. If, therefore, milk is withheld, children are likely to get too little calcium and growth may suffer in consequence. Other fats than those of milk contain very little of the fat-soluble vitamin which has been shown to be so essential for healthy growth. A statement like that appearing in a recent textbook to the effect that milk has killed more children than it has saved ought not to be allowed to pass unchallenged. The observations of McCollum in Baltimore, whose work many of you have no doubt seen, have demonstrated the remarkable effects on growth, weight and activity, from the addition of one quart a day to the diet of children in an orphan asylum who had previously had no milk.

I regret that Dr. Hoobler has taken such strong grounds in his paper. Children from whose diet milk has been excluded or given in very small amounts after infancy seldom, in my observation, exhibit the best types of physical development.

DR. HOOBLER: Dr. Kerley has been brave enough to mention acidosis; I rather sidestepped that word and used the words acetonuria with recurrent vomiting, and in the discussion of evil effects of boiled milk I might have omitted rickets, scurvy and tetany, but I do think boiling milk is a contributing etiologic factor in these conditions, and one we should recognize and protect against.

Dr. Ladd has spoken of butter fat. The difficulty is that butter is put into broths and sauces and spread on bread, so that we do not realize how much fat the child is really getting in the form of butter.

Dr. Holt has given a good suggestion. I should not want to give the impression that we want to eradicate milk from the diet. I think that a child over a year of age, getting other food, should have at least a pint of milk a day and not a quart as some have been teaching in the lay press. A first rate slogan might well be "At least a pint of milk a day for every child."

LESIONS IN THE MIDBRAIN

REPORT OF A CASE

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Although the midbrain is one of the smallest divisions of the central nervous system, within its structure are to be found certain essential nuclear centers and great nerve paths, motor and sensory, connecting the cerebrum and cerebellum with the spinal cord and thence with the entire nervous system. It is the continuation upward from the pons varioli and comprises the two crura of the cerebrum which are surmounted by two pairs of tubercles; the corpora quadrigemina. The aqueduct of Sylvius, connecting the third and fourth ventricles, penetrates its entire length on its dorsal aspect.

Its principal nuclear structures, in addition to the quadrigeminal bodies, are the two large paired red nuclei, receiving fibers from the superior cerebellar peduncles, the nuclei of the third and fourth cranial nerves, the central gray nuclei, the small nuclei of the fifth nerve, the nuclei of the posterior commissure of the posterior longitudinal bundles and the substantia nigra. At its upper border the midbrain is in close relation to the thalamus and the geniculate bodies.

Because of its central position and of the compactness of its structure, the region of the midbrain presents a difficult field for experimental study. The changes, therefore, in this area brought about by injury and disease have furnished more important information of the function of the several elements composing the midbrain. Extensive lesions in the midbrain are difficult to interpret because of the many complicated connections involved.

The topical diagnosis of lesions in this area has been exhaustively treated by Marburg.[1] Many of the deductions from the reported cases are somewhat conjectural. It is difficult, of course, to distinguish between symptoms that may be due to the destruction of nerve tissue by disease and those which are produced by alteration in function in the same area because of the involvement of neighboring structures.

1. Marburg: Wien. klin. Wchnschr. **18**:532, 1905.

From the mass of often confusing data three more or less outstanding syndromes have emerged as the result of disease in various portions of the midbrain. These are:

(*a*) Syndrome of Weber,[2] which consists of hemiplegia in one side of the body with oculomotor palsy of the other side. This results from a lesion affecting one of the peduncles, due usually to thrombosis of the basilar artery, to tumors or to inflammatory products in this region, and extending mediumly so as to compress the third cranial nerve or its nucleus.

(*b*) Syndrome of Benedict,[3] which consists of the Weber syndrome plus a tremor on the side of the hemiplegia, that is, some oculomotor palsy with a crossed hemiplegia and a persistent tremor which increases somewhat on voluntary motion. Apparently, there is some uncertainty as to the site of this lesion but it probably represents the involvement of the peduncle and the third nerve, the lesion also reaching dorsally to the red nucleus which receives nerve fibers directly from the cerebellum. If the lesion fails to involve the peduncles the hemiplegia may be absent.

(*c*) Syndrome of Nothnagel,[4] which is described as a unilateral or bilateral oculomotor palsy with ataxia of the cerebellum type. It is supposed to suggest the lesion of the corpora quadrigemina with pressure upon the superior cerebellar peduncles. Symptoms of this character are more often the result of tumor in the corpora quadrigemina or in the pineal gland.

In view of the confusing symptomatology often noted in patients suffering from midbrain lesion it will be of interest to report a case in which the symptoms were comparatively definite and the pathologic findings fairly circumscribed.

REPORT OF CASE

The patient was a colored boy, R. J. [No. 6747], 3 years of age who was brought to the Harriet Lane Home, Johns Hopkins Hospital, Feb. 3, 1915, because of "general weakness and trembling and drooping of the eyelids."

Family History.—The family history was negative; the father and mother were well; one sister and one brother were living and well; a brother died

2. Weber: Med. Chir. Trans., 1863, cited by Jelliffe and White: Dis. Nerv. System, Ed. 3, p. 542, 1919.

3. Benedict: Nerv. Pathol., 1872, cited by Jelliffe: Interstate M. J. **18**:819. 1911.

4. Nothnagel: Brain (July) 1889; cited by Marburg.

of pneumonia at 10 months. There had been no other pregnancies and no history of syphilis or tuberculosis or of any illness in the family similar to that of the patient.

Personal History.—The child was born at full term without instruments and was breast fed for fourteen months. He had measles at 18 months and pertussis at 2½ years with uninterrupted recoveries. There have been no other illnesses and no sore throat or skin eruptions. The boy's development was normal. He cut his first teeth at 4 months, walked well at 11 months and talked at 17 months. There have been no disturbances of digestion and no renal symptoms.

The patient appeared to be perfectly normal until six months before admission when he stopped crying almost completely. Nothing further unusual was noted, however, until four months afterward when it was noted that his hands would shake when feeding himself. No paralysis or weakness had been remarked up to this time. At about the same period and following a coryza the mother noticed that the boy's eyes began to droop; both sides were equally affected. The child became nervous, jumped at every noise but no other change was observed except that he did not cry. The mother thought him "as bright as before."

Physical Examination.—When seen the child's general condition seemed excellent. His temperature was 99.6 F.; the skin was clear; his head was well formed; the circumference being 19½ inches. The fontanels were closed. No abnormalities were detected about nose, ears or throat. The teeth were in excellent condition. There was some enlargement of the epitrochlear glands.

Eyes: The pupils reacted to light, the left better than the right. There was an occasional lateral nystagmus of the right eye. A marked bilateral ptosis of the eyelids, apparently equal on both sides, was present. There was definite lateral deviation of the eyeballs to the right. Upward deviation was not well observed; downward deviation seemed normal. There was no conjunctivitis or photophobia.

The lungs, heart and abdomen presented no abnormalities. No definite weakness of the muscles of the legs or arms could be shown—sensation was normal. No alteration was found in the deep reflexes, except that those at the knee were somewhat increased. His gait seemed normal and he executed the finer movements well. Romberg's sign was absent. The boy seemed unusually bright. He obeyed commands well and was not irritable. The Wassermann reaction was negative.

Later Examination.—Two weeks later the patient returned with the history of having had two attacks of weakness (paraplegia), and that he had become very weak and limp after the second one. He was admitted to the ward, February 18. Three days afterward he became somewhat drowsy and difficult to arouse. Macewen's sign was suggestive. There was an increase of ptosis of the right eyelid which he could not raise as well as the left.

When placed on the floor, he stood with his head thrown back, arms outstretched and the feet far apart. When attempting to walk there was great uncertainty of movement and when standing or walking there was a coarse tremor of both arms and legs.

There was no movement of the eyeballs, excepting those produced by the action of the external recti. The examination of the fundi showed a very slight degree of secondary atrophy. There was no evident impairment of hearing.

Laboratory Examination.—The spinal fluid obtained was under a marked increase in pressure, gave a reaction for globulin and contained an increased number of cells mostly of the mononuclear type. On subsequent examinations the number of cells increased from 38 to 200 per c.mm. The Wassermann reaction in the blood and spinal fluid were negative. The von Pirquet test was frankly positive.

Roentgenoscopy.—The roentgen-ray examination of the head showed a moderate internal hydrocephalus and a probable tumor above the sella turcica. March 1, ten days after admission, a slight rigidity of the neck was noticed

Fig. 1.—Bilateral ptosis and external strabismus of right eye due to unbalanced action of external oblique muscle.

for the first time and from this time on the child grew constantly weaker. He was no longer able to support his weight on his feet. His respirations became shallow and irregular. There were slight daily fluctuations of temperature of about 2½ degrees. The external strabismus of the right eye became more marked; the ptosis continued more prominent in the right eye than in the left eye—the pupils reacted slightly to light. The ataxic movements of the hand were still noted when the child attempted to reach for objects.

The drowsiness gradually deepened. March 9, he had the first of a series of general convulsions, which continued daily until his removal from the hospital against advice March 15. No tubercle bacilli were found in the spinal fluid on repeated examinations.

He died at his home March 18, after being under observation forty-two days.

Comment.—The acquired ptosis and the curious tremor of long standing noted in the extremities and the gradually developing paralysis of the movements of the eyeballs excepting those produced by the external recti, with resulting external strabismus, occurring spontaneously in a child previously well, lead one to venture the diagnosis of tumor of the midbrain, interfering with the nuclei of the third and fourth cranial nerves. The ataxia might also be accounted for by lesion in this area, involving the red nucleus or cerebellar tracts. Toward the end there was certainly meningitis, probably of tuberculous origin, associated with hydrocephalus, although the tubercle bacilli were not demonstrated. The positive von Pirquet reaction and the subsequent development of meningitis suggested that the initial lesion in the midbrain was probably tuberculous in origin.

Necropsy 4310. March 19, 1915. Dr. Holmes:

A plastic exudate was found over the base of the brain, extending up to the roof of the fourth ventricle; fine tubercles were seen along the course of the blood vessels about the base and on the surface of the cerebellum. A solitary tubercle, 0.6 cm. in diameter, surrounded by a reddened zone, the whole having a diameter of 1 cm. was found in the tip of the temporal lobe. Dissection of the brain stem disclosed a large tubercle the size of a hickory nut which took the place of the upper surface of the midbrain, the colliculi. The foramen of Magendie was patent, but the surrounding cisternae were plastered down by exudate. The velum intrapositum was thickened, especially on the right.

I am indebted to Dr. Adolf Meyer for the following description, gross and microscopic, of the tumor:

REFORT ON EXAMINATION OF TUMOR

The tumor of the midbrain extends backward and inflates the whole roof so that the frenulum disappears and the two fourth nerves come out from the side of the tumor. On the forward side, the tumor has a thickness of about 18 mm., while the breadth is about 32 mm. The anterior end raises the epithalamus and superior commissure, pineal gland and pineal recess exactly 10 mm. from the transverse ridge of the posterior commissure. The midbrain ventricle is only compressed but not occluded. The whole region was cut horizontally so as to expose the third nucleus of each side.

Microscopic Description.—The tumor at a level just underneath the midbrain or aqueduct takes up nearly the whole right side of the midbrain from close to the median line to the region of the lateral fillet. In the posterior part some motor cells are preserved in tissue partly invaded by the tubercle (region of fourth nucleus) but the more anterior part of the third nucleus is invaded and completely destroyed.

The left third nucleus is not invaded, at least not in its more lateral part. There is no evidence of clean cut and limited destruction of any portion which could be made responsible for the ptosis of that side. It is more likely that we have to account for the motor restriction by pressure. Practically all the cells show dissociation of the Nissl bodies of the nature of fever alteration which reduces the possibility of distinguishing the normal and abnormal cells. Below the level just described the tumor terminates above the red nucleus without, however, invading it definitely.

In the central part of the tumor there are diffuse islands which have lost all nuclei. Only along the blood vessels are there evidences of cellular infiltration and residual tubercles. In the more superficial part of the tumor there is less necrosis and there is a fairly large number of characteristic giant cells. Tubercle bacilli could not be stained in the rather old specimen. On the surface the pia shows meningitis infiltration.

The anatomic diagnosis is solitary tubercle of the midbrain and right parietal lobe, tuberculous meningitis.

Comment.—The anatomic findings confirm, in the main, the clinical diagnosis and account for the symptoms present, although the bilateral character of the ptosis and the paralysis of the ocular muscles would have been more easily accounted for if the destruction of the third and fourth nuclei could have been demonstrated on both sides. However, a mass of the size described must exert marked pressure with interference of function in the adjacent structures not directly involved in the tumor. This fact with the well known collateral connections between the oculomotor tracts may satisfactorily account for the bilateral symptoms. In regard to the ataxia, tremor, it is unwise to make any dogmatic statement in the presence of tubercular meningitis with increased cranial pressure. As, however, the peculiar ataxic tremor of the hands was noticed among the very early symptoms, it is not unlikely that they were produced by the primary lesion, the tuberculoma in the midbrain.

The general weakness and ataxic gait which came on later were probably the result of the meningitis and increased cerebral pressure.

The occurrence of tremors in cerebral lesions has been discussed by Gordon Holmes.[5] From data from sixty cases with necropsy find-

5. Holmes, G.: Brain **27**:327, 1904.

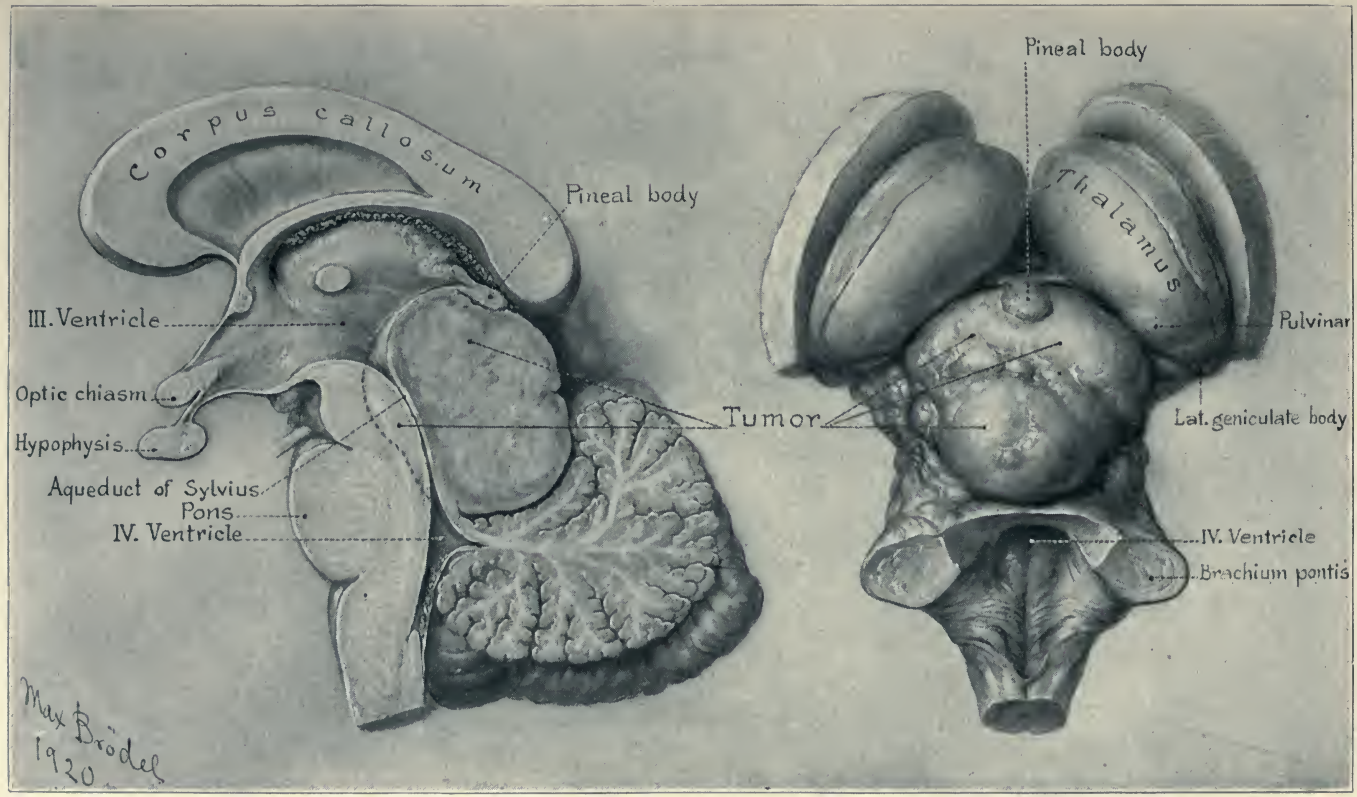

Fig. 2.—A. Sagittal section, showing the extent of the tumor, narrowing but not occluding the aqueduct of Sylvius. Most of the growth is on the right of the median line. The pineal gland is not involved. B. Sketch of the roof of the midbrain showing the displacement of the colliculi by the tumor and its relation to the thalamus and pons.

ings he concludes that the movements are athetoid when the thalamus is involved, are chronic when the midbrain and ganglia are involved and true tremor when the lesion is in the midbrain itself.

Jelliffe [6] considers that choreiform and chorei-ataxic movements are the result of a lesion in the midbrain with the involvement of the superior cerebellar peduncles, whereas those tremors suggesting paralysis agitans arise from involvement of the red nucleus.

It would seem more probable that the choreo-ataxic tremor noted in my case might be associated with involvement of the superior cerebellar peduncles, as the growth itself did not reach the red nucleus.

Tumors limited strictly to the corpora quadrigeminal bodies must be extremely rare. The symptoms produced by a growth beginning in this area are due to the involvement of the underlying structures.

Ferrier and Turner [7] have shown that destruction of those bodies in monkeys does not result in any permanent phenomena and that the colliculae themselves apparently have a small functional value.

Among the rather infrequent cases, similar to mine in the literature should be mentioned those of Nissen,[8] who out of the large clinical material of Elizabeth Hospital, St. Petersburg, has reported five cases in which the diagnosis of tubercle of the midbrain was made and in three confirmed at necropsy. In the first case, a boy of 3 years, the principal symptoms were a gradually increasing ptosis of the right eyelid—later of both sides—oculomotor paralysis becoming complete, and a spastic paralysis of the left extremities. On section there was found a large caseous mass in the right side of the midbrain, involving the cerebral peduncle and extending nearly to the roof so as to invade the oculomotor nuclei. There was no meningitis and only moderate hydrocephalus.

In the second case, a child 19 months old, certain additional symptoms were noted, namely, some stiffness of the neck and diminution of vision. These were explained by pressure in the medulla and by the extension of the caseous tumor into the optic thalamus.

The fifth case, a child 5 years old, had symptoms suggesting a tuberculosis of the brain with paralysis of both sixth nerves and optic neuritis. At necropsy an extensive tuberculous exudate involving the

6. Jelliffe: Interstate M. J. **18**:817, 1911.
7. Ferrier and Turner: Brain **24**:27, 1901.
8. Nissen: Jahrb. f. Kinderh. **54**:618, 1901.

sixth nerves was found and complete destruction by caseous material of the corpora quadrigemina, to which no definite symptoms could be attributed.

Nissen is of the opinion that tumors of the midbrain proper tend in their earlier stages to produce only localized effects, that the general symptoms of brain tumor referable to increased intracranial pressure, such as headache, vertigo and optic atrophy, are more prone to follow tumors in other parts of the brain. He calls attention to the fact that several tuberculous masses are twice as likely to occur in the brain as is a single solitary tubercle.

Hoppe [9] has reported a case of a girl, 17 years of age, who died after an illness of a year as the result of a tumor in about the same situation as that of our patient. The principal symptoms were headache, double vision, ending in four months in total blindness; ataxia, staggering gait, paralysis of the external recti of both eyes, slight ptosis of both eyelids and atrophy of the optic nerve. There was no defect in hearing or alteration in sensation. On necropsy, a gliomatous mass, 2 by 4 cm., was found involving the corpora quadrigemina and extending back into the left cerebellar hemisphere. The nuclei of the third and fourth cranial nerves were involved but the blindness was due probably to the papilledema of the optic nerve brought about by the increased intracranial pressure. This hypertension also exerted on the nerve trunk of the sixth nerve might explain the paralysis of the external recti. This case confirms the experimental evidence and the contention of Nissen and others that neither blindness, deafness, nor ataxia are pathognomonic of the disturbed function of the quadrigemina.

Another important structure in close proximity to the midbrain must be considered briefly, namely, the pineal gland, which lies immediately upon the anterior corpora quadrigemina.

The pineal gland is the seat not infrequently of hypertrophy, tumors, cysts and various degenerative changes which may exert pressure on the subjacent structures. The quadrigeminal bodies may be flattened or destroyed and the whole midbrain greatly distorted by these masses springing from the pineal gland.

The anatomy, physiology and pathology of the pineal body has been extensively studied. Bailey and Jelliffe [10] have collected a large series

9. Hoppe: J. Nerv. & Ment. Dis. **39**:108, 1912.
10. Bailey and Jelliffe: Arch. Int. Med. **8**:851 (Dec.) 1911.

of tumors of the pineal gland and Kidd [11] in 1913 summarized all the data bearing upon the body. These writers and Skoog [12] discuss the metabolic changes which may reside in the pineal gland.

It has been claimed that adiposity and the development of premature sexual characteristics result from interference with the function of the pineal gland. The reference of these changes directly to the pineal body must be accepted with reserve, as Park [13] has pointed out that of the seventy cases of pineal gland tumors reported symptoms of precocious development appear in but five and excessive growth in but seven, and that it is quite possible that the occasional results may be due to secondary alterations of neighboring structures, as for example the pituitary.

The neurologic signs and symptoms, however, resulting from pineal tumor must be considered in discussing the affections of midbrain injury. Among them are headache, increased intracranial pressure, often with hydrocephalus, giddiness, nausea, drowsiness, isolated eye palsies, ataxic gait and tremor. It is evident that many of these symptoms are identical with those produced by primary lesions of the midbrain.

The order in which certain localizing symptoms develop is of the utmost importance in reaching an accurate diagnosis. When the early symptoms are general and attributable to increased cerebral pressure, such as headache, vomiting, optic atrophy, hydrocephalus, etc., followed, perhaps, by ptosis and oculomotor palsies, one would be inclined to place the initial lesion outside of the midbrain—such symptoms might result from meningitis or tumor elsewhere, possibly originating in the pineal gland. Whereas, as in the case here reported, the limitation of the symptoms for months to ptosis and paralysis of the oculomotor nerves and tremor without evidence of increased intracranial pressure support the diagnosis of an injury beginning in the midbrain, and as far as it goes, the absence in my case of any increased rate of growth or of sexual development suggest that neither the pineal nor pituitary glands were involved.

I take pleasure in thanking Dr. Adolf Meyer for his kindly interest and assistance in describing the specimen, and Dr. John Howland for the opportunity of reporting the case from his wards, and Mr. Max Broedel for the accurate drawings.

11. Kidd: Neurol. & Psychol. **11**:1, 1913.
12. Skoog: Tr. Sect. Nerv. & Ment. Dis., A. M. A., 1918, p. 241.
13. Park: Am. J. Dis. Child. **12**:477 (Oct.) 1916.

MALT SOUP EXTRACT AS AN ANTISCORBUTIC*

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During 1918, while studying the respiratory quotient of scorbutic infants, we decided for definite reasons to feed these infants with Keller's malt soup, a mixture containing 100 gm. of the so-called malt soup extract, which has made for itself a record of producing and never of curing scurvy. Hess,[1] for instance, reports that in his experience the malt soup preparation is the diet which has been associated with scurvy most frequently. September 6, 1918, a patient who had developed a scurvy in another institution on Keller's malt soup was given the same kind of a mixture in pursuance of the above stated aim, but on the fourth day orange juice was added to the diet, and so the surprise which we were to have later in the case of another patient was inadvertently postponed. September 26, 1918, another scorbutic patient, 11 months of age, was brought to the hospital with a history of poor development and bad stools (Table 1). He was bottle-fed since birth. From the age of 1 month on until he was 10 months old he was fed a mixture of one-half milk and one-half oatmeal water with cane sugar. Then he received for another month two-thirds milk and one-third oatmeal water. During this month he suffered from diarrhea, and as a result, the stepmother, who took charge of him at this time, frequently gave him castor oil, but without beneficial effect on the painful lower extremity. The physical examination showed a decided case of scurvy, the patient having swollen and bleeding gums about the upper and lower incisors, enlarged epiphyses, a rosary, an enlarged spleen, and increased permeability of capillaries, a swollen right knee and a very sensitive left knee. For our purposes of respiratory quotient study he was also put on Keller's soup. On the day of his admission to the hospital he received a mixture of one-half skimmed milk and one-half oatmeal, and on the following day he was offered Keller's soup, but refused most of it, taking only a total of 250 c.c. On the next day, however, he took 820 c.c. and then the full 1,000 c.c. offered him. We expected no improvement, and as we wished to see the effect of the

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1. Hess. Alfred F.: Infantile Scurvy. V. A Study of Its Pathogenesis. Am. J. Dis. Child. **14**:347 (Nov.) 1917.

orange juice on the respiratory quotient and as we also wished to have the same carbohydrate intake in the preliminary period as would occur in the regular period, we gave him, besides 1,000 c.c. of Keller's soup, 60 c.c. of a 10 per cent. solution of sugar, composed of 6.5 per cent. of glucose and 3.5 per cent. of sucrose. The higher percentage of glucose was used because levulose was not available.

TABLE 1.—ANALYSIS OF CLINICAL HISTORY OF SECOND SCURVY PATIENT

Date, 1918	Food		Weight, Gm.	Temperature			Stools	Clinical Condition and Symptoms
	Kind	Amt., C.c.						
Sept. 26	Skimmed milk ½, OMW ½	600	.....	38.1	37.6	27.6	E	Pallor; restless; bleeding and swollen gums about incisors; right knee swollen and very sensitive, left also sensitive. Child also showed a marked rosary, enlarged spleen and epiphysis on admission; had diarrhea for a long time before admission
Sept. 27	Skimmed milk ½, OMW ½	100	5,610	38.2	37.8	37.9	1 T	Same
	Keller's soup	250						
Sept. 28	Keller's soup	820	5,480	37.0	37.3	38.0	3 T	No change noticed
Sept. 29	Keller's soup	1,000	5,550	37.9	37.6		3 T	No special observation made
Sept. 30*	Keller's soup	1,000	5,725	36.6			2 N	
Oct. 1	Keller's soup	1,000	5,855	36.8			1 T	Child's improved disposition noted
Oct. 2	Keller's soup	1,000	5,845	37.0	37.4		2 N	Gums normal; joint sensitive and swelling gone
Oct. 3	Keller's soup	1,000	5,800	37.0	37.6		5 N	Same; very happy; looks much better
Oct. 4	Keller's soup	1,000	5,790	37.2	37.6		4 N	Same; joints negative to pressure
Oct. 5	Keller's soup	1,000	5,800	37.4	37.6		3 N	Continued general improvement
Oct. 6	Keller's soup	1,000	5,800	37.9	37.9		2 N	
Oct. 7	Keller's soup	825	5,790	37.0	37.2		1 SN	
Oct. 8	Keller's soup	100	5,900	37.2	37.2		2 T	
Oct. 9	Keller's soup	100	5,970	37.0	37.0		1 SN	
Oct. 10	Keller's soup	100	5,945	36.8	37.8		2 N	
Oct. 11	Keller's soup	100	5,900	37.2	36.2		1 SN	
Oct. 12	Keller's soup	100	5,950	37.4	37.4		2 SN	Color better

* September 30, the patient received 60 c.c. of a 10 per cent. sucrose solution; October 1 to 7, inclusive, 90 c.c. of a solution containing 3.5 per cent sucrose and 6.5 per cent. glucose daily; October 8 and 9, 660 c.c. and October 10, 11 and 12, 90 c.c. of the same solution daily.

October 1, it was noticed that the child seemed different, but no particular attention was paid to the scorbutic symptoms, simply because we did not expect any special change. October 2, however, the child seemed so normal that an accurate inspection of the gums was made, and to our great surprise these were found to be absolutely normal. The swelling of the right knee joint had lessened, and the sensitiveness of both the left and the right knee had practically gone. With each succeeding day the child improved in general appearance and dis-

position, so that we could say definitely that the child had been cured of scurvy, at least of the severe, active stage of scurvy. This experience was so remarkable that nothing was said about it and observations were made to determine whether through some error the child had not received an antiscorbutic. No evidence in this connection was discovered, however, and so it was decided to say nothing and wait for the next opportunity, which came Dec. 13, 1918.

This third patient had an enormous hematoma of the right femur, and after three days of half milk, half oatmeal water, and 2½ per cent. of cane sugar, the child was given Keller's soup, prepared with the same malt extract that had been used in the previous cases. The gums of this child were perfectly normal, and we had to depend entirely on the sensitiveness and the size of the large swelling to decide whether we had much improvement or not. After three days' observation there was no definite and positive improvement, and as the child was quite ill and had a temperature of 38.5 C., and as the respiratory quotient curves showed certain interesting features, we decided to give orange juice at this time, with the result that within a few days the child showed a distinct improvement. But the improvement was gradual, even with 90 c.c. of orange juice in twenty-four hours, so that, after all, we did not know from his experience whether or not the Keller's soup or the malt extract in the Keller's soup had also exerted any antiscorbutic influence in this child. So again we decided to wait for another opportunity, which came Dec. 30, 1918.

This fourth patient, a colored infant, 10 months of age, was brought to the hospital with a history of stomach trouble and swollen feet (Table 2). She had been artificially fed since the third week, at first for six weeks with a milk dilution, then for six months with bread and tea, and finally during the last three months with a cane sugar one-half milk and one-half water mixture. On physical examination the child showed a very marked rosary and a decided swelling of the lower extremities—especially below the knees. All the tissues about and especially above the right ankle were very much indurated, and all of these swollen areas were extremely sensitive to the slightest pressure. The child objected to moving its legs and was very unhappy and irritable. The gums showed no lesions, even though too small lower incisors had just erupted. This finding is not so very uncommon in cases of scurvy, especially as regards the lower incisors, and in no manner speaks against the correctness of the diagnosis of this case. We have had occasion to see undoubted symptoms of scurvy develop, when the gums

of both the lower as well as of the upper incisors were normal. It is unquestionably true, however, that swollen, bleeding, bluish-red gums are the most dependable and characteristic sign of infantile scurvy. The epiphyses at the wrists were only slightly enlarged. After three

TABLE 2.—ANALYSIS OF CLINICAL HISTORY OF FOURTH SCURVY PATIENT

Date, 1918	Food		Weight, Gm.	Temperature			Stools	Clinical Condition and Symptoms
	Kind	Amt., C.c.						
Dec. 30	OMW ⅓, milk ⅔, cane sugar 3%	700	.....	37.3	37.5	37.1	...	Marked fretfulness and restlessness; pain on the slightest movement of lower extremities; decided swelling and induration of tissue above knee and especially below; marked sensitiveness to slightest touch; gums normal. Child shows a very marked rosary
Dec. 31	OMW ⅓, milk ⅔, cane sugar 3%	900	5,370	37.6	37.2	37.6	1 N	Same
Jan. 1	OMW ⅓, milk ⅔, cane sugar 3%	700	5,370	38.0	37.1	37.6	1 N	Same
Jan. 2*	Keller's soup	900	5,175	36.4	36.6		3 N	Same
Jan. 3	Keller's soup	900	5,145	36.6	37.2	36.6	6 SN	Disposition seems better; urinates more
Jan. 4	Keller's soup	900	5,130	36.2	36.5		3 SN	Seems more comfortable; urination much incr.
Jan. 5	Keller's soup	900	5,100	36.6	37.5		3 SN	Less sensitive; wet all the time
Jan. 6	Keller's soup	900	5,130	37.0	37.2		3 SN	Swelling practically gone; sensitive only to deep pressure; happy
Jan. 7	Keller's soup	900	4,925	36.6	37.4		2 N	Laughs and is contented; still very wet
Jan. 8	Keller's soup	900	4,905	36.5	36.6		2 N	Legs show no swelling whatever; no pain even on deep pressure; seems entirely well
Jan. 9	Keller's soup	900	4,870	36.5	37.2		4 N	
Jan. 10	Keller's soup	900	4,840	36.1	37.2		2 N	
Jan. 11	Keller's soup	900	4,900	36.1	37.1		2 N	
Jan. 12	Keller's soup	900	4,850	36.0	36.5		2 N	
Jan. 13	Keller's soup	900	4,910	36.6	37.6		2 N	
Jan. 14	Keller's soup	900	4,850	36.1	37.0		3 T	
Jan. 15	Keller's soup	900	4,910	36.6	37.3		1 N	
Jan. 16	Keller's soup	900	4,800	36.5	37.3		1 N	
Jan. 17	Keller's soup	900	4,990	36.8	38.0	36.0	2 N	
Jan. 18	Keller's soup	900	4,990	36.5	37.5		1 N	Pertussis vaccine; left knee and right ankle sensitive to pressure; is fretful. Due to effects of vaccine injection

* From January 2 to 8, inclusive, the patient received 90 c.c. of artificial orange juice daily and from January 9 to 18, 90 c.c. of orange juice daily.

days feeding with two-thirds milk and one-third oatmeal water, with 3 per cent. cane sugar, during which time no improvement was noticed, she was given Keller's soup made up with the same malt soup extract that had been employed for the last two cases. Ninety c.c. of artificial orange juice were also given. The next day, January 3, the infant

seemed to be passing more urine, and especially was this difference noted the following day. No attempt, however, was made to get an accurate record of the amount of urine excreted, as the patient was a little girl. After twenty-four hours of Keller's soup the child's disposition seemed to be changed for the better, and January 5 there was a

TABLE 3.—ANALYSIS OF CLINICAL HISTORY OF FIFTH SCURVY PATIENT

Date, 1919	Food		Weight, Gm.	Temperature			Stools	Clinical Condition and Symptoms
	Kind	Amt., C.c.						
May 10*	S. M. A.	250	.....	.....			1 SN	Pallor, fretfulness, marked swelling of right ankle and thigh; knees and ankles sensitive to slightest touch; suppurating hematoma in right buttock. Râles at both bases
May 11	S. M. A.	490	7,170	39.7	38.8	39.6	2 SN	Same
May 12	S. M. A.	390	7,340	40.2	38.0	39.0	3 SN	General condition decidedly better; no local change
May 13	S. M. A.	690	7,260	37.7	39.4	38.4	2 SN	Much improved generally; looks about
May 14	S. M. A.	790	7,220	39.0	38.5	37.5	3 SN	Marked increase in urination; even more comfortable. Still breaths rapidly, looks "pneumonic"
May 15	S. M. A.	970	7,430	39.4	38.8	39.2	3 SN	Marked increase in urination; swelling of right ankle gone entirely; legs can be moved with little discomfort; tries to smile. Pseudolabor pneumonia at left base
May 16	S. M. A.	960	7,210	38.3	39.4	37.7	5 T	Right ankle also much reduced; sensitiveness of joints practically gone; smiles. While scorbutic symptoms have markedly improved, pneumonic picture remains unchanged
May 17	S. M. A.	970	7,290	39.5	38.4	38.6	5 T	Child moves legs about of own accord without pain; no tenderness except in right hematoma area
May 18	S. M. A.	900	7,330	38.4	39.5	38.0	3 T	Is interested and can smile
May 19	S. M. A.	905	7,620	39.5	39.5	38.0	3 T	
May 20	S. M. A.	960	7,550	37.0	37.6	38.2	3 T	Pneumonia picture changed
May 21	S. M. A.	950	7,340	37.4	37.4	36.8	5 SN	Pneumonia picture gone
May 22	S. M. A.	1,000	7,320	36.9	37.0	37.1	1 N	
May 23	S. M. A.	990	7,330	37.0	36.8	36.4	4 SN	Right thigh still slightly tender; healing of suppurative hematoma. Looks fine; seems very well; few räles still present at left base
May 24	S. M. A.	985	7,340	36.6	37.2	37.5	6 SN	
May 25	S. M. A.	985	7,295	36.8	36.9	37.5	5 SN	
May 26	S. M. A.	885	7,295	36.8	37.4	37.7	8 SN	

* May 10, the patient received 60 gm. of malt soup extract, and from that day on, 100 gm. daily.

marked reduction in the sensitiveness, to pressure on the knees, the tibiae and the ankles. January 6 there was an enormous improvement, the legs being sensitive only to every deep pressure, the swelling and induration having practically disappeared. The baby moved its legs about and appeared to be all right. January 8 no swelling whatsoever

could be found, and even severe pressure brought no response; the baby laughed and was very happy and contented. So that in this case we can maintain that the child was definitely cured without receiving orange juice or any other hitherto known antiscorbutic. January 9 orange juice was given for respiratory quotient study, but no further change in the condition of the child was noticed, except on the eighteenth, when the child received an injection of pertussis vaccine and as a result developed fever and, what is interesting, a sensitiveness of the left knee and of the right ankle. This renewed sensitiveness, however, disappeared within a few days, and evidently had some direct connection with the injection of the pertussis vaccine.

May 10, 1919, a fifth baby, 8 months old, was brought to Lakeside Hospital with a diagnoss of osteomyelitis (Table 3). The mother stated that the child had been coughing for two weeks, and had also developed at about that time a large swelling on the right buttock, which was opened by a physician. While this wound had drained quite well, the tumor below the abscess seemed to get larger and more tender. The patient was admitted on the surgical service and then taken over to the pediatric service with a diagnosis of scurvy. The right thigh between the knee and hip was markedly swollen and the old incision was still oozing slightly. Both knees and the right ankle were especially sensitive, also the left ankle, but not as much as the other three joints. Around and especially above the right ankle there was marked and hard induration, and through the skin bluish areas could be seen. The child was pale, had a marked rosary of the "necropsy chest" type, enlarged epiphyses at the wrists, was very fretful, laid in a frog fashion, and would cry severely as soon as its lower extremities were moved.

Instead of giving this child Keller's soup we gave it S. M. A. (synthetic milk adapted) in order to exclude the possible therapeutic effect of the one-third certified milk that had been used in the Keller's soup for the other children recorded above. A large batch of 20 quarts of S. M. A. was made at one time and prepared over the regular route of pasteurization. We offered the child 1,000 c.c. of S. M. A., but inasmuch as its appetite was very poor we had to resort to gavage after a few days. The antiscorbutic value of S. M. A. is small, and not adequate to prevent a normal child that is getting nothing but S. M. A. from developng scurvy, so that any therapeutic effect obtained by the giving of S. M. A. could not be explained by its administration. Therefore, in this case we gave the malt soup extract, a part of the same lot

that had been used for the preparation of the other Keller's soup mixture used in the previously described cases, in the same amount in which it had been administered in the form of Keller's soup, namely, 100 gm. for each twenty-four hours. May 11, the child received 60 gm.; May 12, 100 gm., and after that 100 gm. daily were given of the malt soup extract in addition to the 1,000 c.c. of S. M. A. At first the malt soup extract was given separately, later on it was mixed with the S. M. A., just before it was offered to the child, and so it was not exposed to a temperature above 37 C. The subjection of this malt soup extract to a higher temperature would have made no difference, however, because it was exposed to boiling temperature in all of the previous cases, and in all but the last to an additional temperature above 100 C., but it still retained sufficient antiscorbutic value to cure, without question, the second and fourth infants.

When this patient was first admitted it showed besides the lesions already described, râles at both bases, especially on the left side, accompanied with a temperature that varied daily anywhere from 37.8 to 40.1 C. May 15 there was a definite and marked impairment of resonance of the left lower lobe, accompanied by bronchial breathing so that we could make a diagnosis of pseudolobar pneumonia. As a result of this pneumonia, the infant did not make a complete change for the better until May 20. The presence of the pneumonia, however, did not obscure the definite and marked improvement in the scorbutic symptoms after the beginning of the malt soup therapy.

As stated above, May 11 the child received its first malt soup extract, and May 13 there could be seen a marked improvement in the joint sensitiveness. As a matter of fact, some improvement was noted May 12, twenty-four hours after the beginning of the therapy. May 14 a marked increase in urinary excretion was also noted, but inasmuch as the fluid intake was low, owing to the poor appetite of the child and its resistance to gavage, the increased urination may have been due more to the increased intake rather than to any diuretic effect of the malt soup extract, although, in all probability, the latter was a factor when one considers that the other children did take more fluid before they received their malt soup extract in the form of Keller's soup and, nevertheless, showed a marked increase in urinary excretion. May 15 the brawny induration of the right ankle was entirely gone, the tenderness of the left knee was markedly diminished, and the child offered no complaint when the left knee and thigh were flexed on the

abdomen. Only the right thigh, owing to the presence of the suppurating hematoma, was still protected by the infant against too marked a movement, but even this swelling of the right thigh had been reduced in size, and there was also a decided improvement in the general condition of the child. It became interested in things, and, even though it was still very sick with its pneumonia, it tried to smile and would watch objects that were placed before it, something which it had not done before.

On the next day, May 16, the right thigh had reduced in size enormously and the baby was much more improved, as far as its general disposition was concerned; it smiled and the knees could be flexed without causing any pain. The same was true of the ankles. The pneumonia was still causing a rise of temperature up to 39.5 C., giving beautiful proof that the improvement was due to something different than a change in the condition of the lungs, which clinically could not be recognized. To our great surprise and amazement it was learned from the history that this infant had received nothing but its mother's breast-milk. No oranges, tomatoes, potatoes or any other foodstuffs were given it. The mother herself was well, had had no bleeding gums, no painful extremities, and had been eating a general diet, including potatoes. This child was the result of the sixth pregnancy, the first two having ended at six months, while the third, fourth, and fifth went to full term and brought forth infants who are living and well.

We appreciate fully that this history raises a justified doubt as to whether the symptoms in this child were due to scurvy. And yet, after considering the physical findings and the type and course of improvement in the picture after the giving of the malt soup extract, on the one hand, and, on the other, the great improbability that under the same treatment such a marked and rapid change in the condition of the extremities could have occurred if the lesions were due solely to some sort of an infection—we cannot come to any other conclusion than that this case is one of the rare cases of scurvy in breast-fed infants. Possibly when the etiology and the pathogenesis of scurvy will have been clearly established cases such as this one will appear less enigmatic.

So this last patient is also put down as a severe case of scurvy cured in its acute stage by the administration of malt soup extract in a dose of 100 gm. per twenty-four hours, making a total of at least three

cases of severe and unquestionable scurvy, cured by the administration of malt soup extract.[2]

As stated before, Keller's malt soup is a food that is very prone to cause scurvy in infants, and yet there can be no question as to its curative effect in three of the above described cases, an effect that can be dissociated in these severe and yet rapidly cured cases from the quantity of the milk, the heating factor and the ageing factor, as all of these detrimental factors existed in each of the three cases of cure, as the following data will show:

The only factor, besides the malt soup extract itself, that might be considered as having been responsible for the improvement is the quality of the milk, for certified milk was used in the preparation of each batch of food, and it might be imagined that cows producing certified milk are possibly given a diet that would put into the milk more anti-scorbutic substances than would be found in the milk of the ordinary milk cows, which most likely has been used, as a rule, in the making of Keller's soup.

However, neither the fact that certified milk was used, nor the possibility of a greater anti-scorbutic content of such a milk make this idea seem at all probable, as the certified milk used in making the curative Keller's soup for infants came from the same certified dairy from which is obtained the certified skimmed milk which is used in the manufacture of S. M. A. milk, a food which will cause scurvy, even though it contains the same amount of milk as Keller's soup, if no anti-scorbutic is given in addition. And, finally, the food which the cows at the certified farm received was dry and varied in its source, as one would have expected from the fact that the one infant was fed from Sept. 27 to Oct. 12, 1918; the other from Jan. 2 to Jan. 18, 1919; and the third from May 10 to May 26, 1919. So it would be a strange coincidence indeed that cows fed at such widely separate periods on dry food-stuffs, known to have come from different sources, should produce a milk of such high antiscorbutic power that even in the quantity of not more than 330 c.c. for twenty-four hours, boiled, pasteurized, or even sterilized under pressure, and from two to three weeks old, would produce results so paradox to the universal proscorbutic experience with Keller's soup. Therefore, it would seem much more rational to assume that the one and the same batch of malt soup extract which was used in the case

2. The malt soup extract used in this work was labeled 8149 by the Borcherdt Company.

of each of these infants was, in all probability, responsible for the good therapeutic results.

The second infant received Keller's soup which was made with certified milk in the ordinary way by boiling, and which then, in addition, was sterilized under pressure for thirty minutes. The entire batch consisted of thirty-two quarts, and for seventeen consecutive days the patient received exactly the same food, making the last quart eighteen days old.

It may be interesting to note in this connection that the remainder of this lot of Keller's soup which cured this infant of its scurvy, produced a fatal scurvy in a number of guinea-pigs, even though their stools were normal during the earlier half of the experiment and decidedly diarrheic during the latter half, and even though they ate more than enough to meet their caloric and fluid requirements. At the necropsy most of these pigs had their large intestines one-half to two-thirds full of a soft, thin stool.

The fourth infant received Keller's soup, all of which was also made at one time, and the last quart of which was fourteen days old when consumed. This batch of food, however, was not subjected to sterilization under pressure.

Evidently, all of these factors were not adequate to reduce the curative properties of the malt soup extract to a level below immediate and marked therapeutic efficacy.

No conclusive facts regarding the cause of the presence of the antiscorbutic properties of malt soup extract No. 8149 can be given at this time. In the light of our present knowledge, however, there can be only one explanation, as a visit to the factory and a conference with the manufacturer of the malt soup extract convinced me that lot 8149 was alkalinized in the prescribed manner with methyl red as the indicator.

The most probable explanation would seem to us to be that the barley from which the malt used for the manufacture of the malt soup extract was derived, had reached an age and stage of germination at which much antiscorbutic substance was produced, or that the barley grain itself possessed an unusually high amount of potential antiscorbutic material.

Valentin Fürst[3] called attention to the fact that while plain barley,

3. Fürst, Valentin: Weitere Beiträge zur Aetiologie des experimentellen Skorbuts des Meerschweinchens, Ztschr. Hyg. u. Infekt. Krankh. **72**:132, 1912.

oats, peas, etc., have none or not sufficient antiscorbutic powers to prevent the development of scurvy in guinea-pigs, the very same barley, oats, peas, etc., when brought to germination by being kept in a moist warm room for about three days, develop marked and adequate antiscorbutic properties, as tested out on guinea-pigs, and recently in the Chemical Abstracts (April 10, 1919) H. S. Paine[4] reports that E. Weill, G. Mouriquard and Mlle. Peronnet have found that cereal grains of ten days germination age have a greater antiscorbutic value than those of three days old.

If this is the true explanation of the presence of the antiscorbutic factor in the malt soup extract, then it should be possible to use in the manufacture of malt soup extract only malt that has been made from barley of the proper age and state of germination. This would be an addition to our present list of antiscorbutics of another agent of real value as malt soup extract can be used to advantage in other respects in the diets of infants and young children, especially of those that are inclined to be constipated.

The difference in therapeutic results between infants, on the one hand, and guinea-pigs, on the other hand, is undoubtedly due to the decidedly larger antiscorbutic requirements of the guinea-pigs.[5] From the work of Chick, Hume, Skelton [6] we know that a guinea-pig of about 250 gm. weight requires from 80 to 100 c.c. of raw milk daily to prevent the development of scurvy or, at least, to postpone its appearance for a long time, and according to Hess [7] the infant requires about 500 c.c. of raw milk in twenty-four hours. Such infants will weigh on an average at least 5,000 gm.; in other words, twenty times as much as a guinea-pig, and yet infants require only five times as much milk as do guinea-pigs to protect them against the development of scurvy.

This experience with the guinea-pigs and infants fed with the same Kellar's soup would indicate that the antiscorbutic content of

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4. Paine, H. S.: Chemical Abstracts **13**:749 (April 10) 1919. Appearance of an Antiscorbutic Substance During Germination of Cereals. E. Weill, G. Mouriquard, and Mlle. Peronnet, Compt. rend. soc. biol. **81**:607, 1918.

5. Chick, H., Hume, H., and Skelton, R.: Antiscorbutic Principles in Limes and Lemons, Lancet **2**:735 (Nov. 30) 1918 .

6. Chick, H., Hume, H., and Skelton, R.: Antiscorbutic Value of Milk in Infant Feeding, Lancet **1**:1 (Jan. 5) 1918.

7. Hess, A. F., and Unger, L. J.: Factors Affecting the Antiscorbutic Value of Foods, Am J. Dis Child. **17**:239 (April) 1919.

the malt soup extract was relatively not as great as that of orange juice or tomato juice, although it was evidently sufficient to cure severe acute cases of scurvy in infants, and it may well be possible that a malt soup extract could be manufactured whose antiscorbutic powers would be distinctly greater than those present in the lots used for this work.[8]

CONCLUSIONS

1. A report is made of a rapid and marked cure, such as is experienced with orange juice, of three cases of severe infantile scurvy by the administration of 100 gm. of malt soup extract. In two of these the malt soup extract was given in the form of Keller's soup, in the third, in conjunction with S. M. A.

2. The explanation offered for the presence of the antiscorbutic property in this No. 8,149 lot of malt soup extract is that it was, in all

8. Since this article was submitted, the remainder of lot 8,149 was given to three infants, two of whom had clear-cut cases of scurvy, while the other never got beyond what at most could be called a subacute form. The data obtained were inconclusive and consequently are of no value. In the last mentioned child, seen during September, 1919, an otitis media, a pyelitis and a probable enteritis follicularis were responsible for the poor condition and the lack of improvement. The malt soup extract was given mainly together with S. M. A., but for five days it received it in the form of Keller's soup made with certified milk which came from the same farm that produced the milk used in the feedings for the cured cases presented in the article.

The first child had a clear-cut scurvy and came to the hospital during a severe hot spell in July, 1919, suffering in addition from a severe dyspepsia. The vomiting greatly limited the amount of malt soup extract retained and as signs of dehydration appeared the observation had to be stopped and the diet replaced by large doses of orange juice, barley water ad libidum and saline infusions with beneficial results.

The other child, 7 months old and weighing 7,000 gm., was seen in November, 1919, ill with a definite scurvy. It received the very last part of lot 8,149, which was just enough for four days. No definite improvement was registered at the end of this time. It was then given for four days 100 gm. of lot 9,322, neutralized with potassium carbonate, which had recently been made at the factory. This also was without beneficial result and so for the next five days 100 gm. of lot 9,322, to which, however, no potassium carbonate had been added at the factory, were administered, but again no betterment was observed. Thirty c.c. of orange juice were given on four different occasions and this brought good results. The symptoms, however, did not disappear as completely and as quickly as usual. It is possible that this child required an especially large amount of antiscorbutic to remain well, as the mother, who is intelligent and who seems dependable, states emphatically that the child got 1 teaspoonful of orange juice daily from his third month on and "did not need any more, because his bowels were all right." This child was fed since its second month on a simple dilution mixture at one of the local infant welfare stations.

probability, made from barley of the proper age and state of germination or from a lot of barley possessing an unusually high amount of potential antiscorbutic material.

3. The suggestion is made that all malt soup extract could be manufactured from barley of an age and state of germination that would insure its large and adequate content of the antiscorbutic factor, and that in this manner another antiscorbutic, of value also in other respects to infants and children, could be added to the list of our regular and dependable antiscorbutics.

DISCUSSION

DR. BRENNEMANN: The interesting point about this paper is the fact that it illustrates again that infantile scurvy is still a mysterious stranger in our midst. So confusing are our data concerning its etiology, that one ceases to be surprised at any new developments. It will be recalled that Czerny even said, "If a baby gets scurvy on a certain milk, change diets." Babies have developed scurvy on the breast and on raw milk and have been cured. I reported one case, in which boiled milk alone effected a cure. It has always seemed to me that individual susceptibility and peculiarity is a large factor. If one puts, say, ten children on a certain diet, one child will, perhaps, develop scurvy. If the food is less antiscorbutic, perhaps two children will develop it, and so on. Again, some children will be cured on a smaller amount of antiscorbutic than others, and some will be cured by a food that is relatively little antiscorbutic, if they have been on one that was even less so. For that reason I should like to know exactly what these children were getting before they had scurvy and before they were given the malt soup. The more we learn about scurvy the more one feels that the present hypotheses do not explain many things in connection with scurvy and the more we admire the wisdom and foresight of the members of the committee of the American Pediatric Society on Infantile Scurvy of which Dr. Griffith was chairman, as shown at that early date in that report. I would also take the liberty to question the diagnosis in at least one of these cases—Case 4. In the first place, we do not have a joint involvement in scurvy, and in the second place, with such marked symptoms as were evidently present in this case, I think one invariably finds an involvement of the gums. I do not believe that the rosary in a case like this would distinguish it from rickets. One would also wonder in these cases whether it was not after all the milk, small though the amount may seem, that in these particular cases contained for them a sufficient amount of antiscorbutic.

DR. GRIFFITH: Those of us who have longer been members of the society will well remember the oft quoted statistics of our collective investigation on the cause of infantile scurvy. In this there was nothing which became more apparent than that there were various different dietetic conditions which were capable of producing the disease. Some of the children developed scurvy on pasteurized milk; some on boiled milk; and some on raw milk. Some recovered when pasteurized milk was changed to raw milk, and some, curiously enough, when raw milk was changed to pasteurized milk. Quite a number developed scurvy on breast feeding. It seemed in the report of the committee that the only conclusion justifiable was that there was something wrong with the diet, but that just what this dietetic error was did not appear clear. It is beyond question, however, that there must

be besides diet a peculiar disposition to develop scurvy seen in a comparatively small number of infants. If this were not the case we would find all the infants fed on a certain mixture or proprietary food developing the disease. Thousands of children are receiving without damage the identical food which in some instances is followed by scorbutus.

In referring to malt soup, I am aware that I am voicing an experience divergent from that of some others; and, of course, this negative evidence does not destroy positive proof. At the same time malt soup has been a very favorite food with me for many years, both in hospital and in private practice, and I have seen not more than two or three children develop scurvy in spite of the fact that no orange-juice had been administered. It is again evident that there is some element other than diet, and malt soup is not to be blamed any more than any other foods.

DR. KERLEY: It is rather surprising to hear Dr. Gerstenberger's observation as I have produced more cases of scurvy with malt soup than with any other method of feeding. Was the milk always boiled?

DR. GERSTENBERGER: In the second case it was boiled and sterilized under pressure.

DR. KERLEY: Malt soup feeding is so frequently followed by scurvy that I feel it is always advisable to use orange juice with it. These cases are very unusual and I am glad Dr. Gerstenberger has reported them.

DR. MILLER: I should like to ask Dr. Gerstenberger how he can attribute antiscorbutic properties to the malt soup if the small amount of milk used with it was boiled. He subjected the milk to heat under high pressure, and that is the peculiar point to me, for boiling milk does not have any effect on the prevention of scurvy, and cannot in the amount present in malt soup (11 fluid ounces).

DR. SOUTHWORTH: Dr. Gerstenberger has advanced a very revolutionary theory and I think we ought to talk it over pretty thoroughly before we convey the impression that malt soup extract is an antiscorbutic. In one institution where we have fifty babies we have been using it quite steadily for some years because we get better results than with lactose. The malt soup is not made up by boiling it with the milk. We have used pasteurized milk and cooked barley water and have added the malt soup to it. We thus get such a preparation as we want for each individual child. We have, however, had repeated outbreaks of scurvy when the institution failed to provide sufficient orange juice or tomato juice. It is absolutely imperative that infants receiving malt soup extract should have orange juice or tomato juice in considerable quantities. We have the feeling that any change in the diet helps to relieve a scurvy. It is quite possible that just a change in some of the ingredients of the food may have helped in producing Dr. Gerstenberger's results. I think it a mistake to let the idea go abroad that malt soup extract is an antiscorbutic to which all other clinical experience, up to the present time, is opposed.

DR. GERSTENBERGER: I am glad Dr. Southworth brought up this point. I am simply reporting my experience with these cases fed with Keller's soup, made with one and the same lot of malt soup extract, and am not claiming that any malt soup extract prevents scurvy. I, too, at the present time, would say "never feed malt soup except with orange juice," but having found that this one special lot of malt soup extract seemingly possessed decided curative antiscorbutic properties, the suggestion logically comes to find out why this lot, contrary to all previous experience, had such marked antiscorbutic properties, and to see if it is possible to make all malt soup extract in a manner that would insure its being adequately antiscorbutic. Under such circumstances, it would

not be necessary to depend upon the mother to give orange juice to prevent scurvy when feeding Keller's soup. It was with this idea in mind that I suggested to a manufacturer to make an experimental batch of malt soup extract from barley that had been allowed to germinate longer than customary. I most emphatically agree that it would be a mistake to allow any manufacturer to state at the present time, or to let the impression get abroad now, that malt soup extract, generally speaking, is antiscorbutic. It is interesting that the two curative lots of Keller's malt soup were boiled and one in addition, sterilized under pressure, and both were made in large batches and fed old.

As regards the diets on which the scurvy developed in these cases, let me say that the first case was fed at a Prophylactic Babies' Dispensary, where it received one quart of a two-thirds milk, oatmeal water, and cane sugar mixture, the milk coming from as fine a Holstein herd as exists anywhere. As the farm producing this milk is interested in making international milk producing and breeding records, and is succeeding, it can be assumed that the food fed the cows is of the best quality. As a matter of fact, from personal observation, I would say that no herd in this country, I believe, is better and "more completely" fed. However, this milk is pasteurized at the farm where it is also bottled. The infants get it on the following morning; in other words, in as fresh a state as it is possible to have it under modern methods of supplying a large city with milk. The second baby, three months prior to coming to the hospital, was fed for six weeks on the same milk. However, this child received a mixture of 500 c.c. milk, 500 c.c. oatmeal water, with cane sugar added; in other words, just a little over one pint of milk. During the last six weeks prior to coming to the hospital it received the same quantity of milk, but not the same quality, the special milk having been replaced by ordinary pasteurized bottle milk.

It really seems as if pasteurized food is more prone to cause scurvy than are boiled or sterilized mixtures. Such experiences as these give one the uncanny feeling that possibly, after all, bacteria in some manner do play a rôle in the production of scurvy. It may be that a certain detrimental flora develops more readily in pasteurized milk, and that, as a result, the child requires more anti-scorbutic substance to neutralize the effect of this flora than would be the case in boiled or sterilized milk, in which such a flora may have been killed off. One can easily see how pasteurization, especially if poorly done, might permit of such a development, and according to our present knowledge it is difficult to see how the different effects of pasteurization on the one hand, and boiling and sterilization on the other, could effect such a change in the chemical or physical factors in the milk as it can the bacteriological.

The third patient was breast-fed, with additional feedings of swieback. I have always been skeptical of scurvy cases reported in breast-fed infants, especially, as was also the case here, with a mother showing no signs of the disease, and yet I am firmly convinced that this child was suffering from a severe case of scurvy, judging from the symptoms—hematoma, in the region of the head of the femur, swollen and tender bones and tissues about the knee and ankle joints, bluish discolorations at the ankles and classical "autopsy chest" rosary—and from the clear and marked improvement which occurred with the giving of the Malt Soup Extract.

Regarding the ages of these children and the condition of their gums, the following may be said: The first patient was 11 months old, and had erupted upper and lower incisors, with markedly swollen, blue, bleeding gums. The second child was 10 months old and showed two lower, central incisors that had just erupted; the gums showed nothing that could be called abnormal.

I am of the opinion that swollen, bluish, bleeding gums about erupted teeth represent the most characteristic and most dependable sign of scurvy. However, I do know from experience, having seen severe scurvy develop, that an infant may present an unquestionable and decided clinical scurvy, with hemorrhage about the long bones and into the conjunctiva, without showing a hemorrhagic condition of the gums, even though the teeth may have erupted. This is especially true of the lower incisors. The upper incisors seem to develop bleeding gums much more readily. The last infant was 8 months old, had no teeth, and showed no changes in the gums.

There is absolutely no question but that these children had a severe scurvy and improved in a remarkable manner without the giving of one of the known antiscorbutics. It may be possible that the one-third quart of milk was responible for the improvement and not this special lot of malt soup extract. However, I cannot help but feel that this special lot of malt soup extract did play a distinct part in improving these children, if it was not entirely responsible for the improved condition.

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